THE JOURNEY TOWARDS ONE-POT EPOXIDATION-CARBOXYLATION REACTIONS OF ALKENES

by

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ABSTRACT

Previously in the Kerton group [1], metal-containing ionic liquids have been investigated for the catalytic synthesis of cyclic carbonates from carbon dioxide and epoxides, which can be prepared via catalytic oxidation of alkenes. This has led to the attempt of a one-pot transformation of alkenes in cyclic carbonates using [BMIm]Cl and manganese salts. A number of parameters were examined in order to obtain optimized conditions for the H_2O_2-mediated epoxidation of alkenes. This has lead to exciting results for the conversion of styrene to styrene carbonate.

Investigation then turned towards the synthesis of bis(amide) compounds, that when paired with a suitable metal, might yield catalysts suitable for one-pot epoxidation-carboxylation reactions. This is based off stable oxidation catalysts such as the TAML-Fe complexes developed by Collins and co-workers [2]. Their stability has been attributed to not only the macrocyclic nature of the ligand but also its amide backbone. Adolph *et al*. [3] also recently reported success in using amide-containing ligands in the catalytic formation of cyclic carbonates from CO_2 and epoxides.

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LIST OF ABBREVIATIONS AND SYMBOLS

BMIm	1-*n*-butyl-3-methylimidazolium
CCS	Carbon dioxide capture and storage
CD_3OD	Deuterated methanol
$CDCl_3$	Deuterated chloroform
CO_2	Carbon dioxide
COSY	Correlation spectroscopy
DHBA	Dihydroxybenzoic acid
DMSO	Dimethyl sulfoxide
EI	Electron ionization
GC	Gas chromatography
H_2O_2	Hydrogen peroxide
HSQC	Heteronuclear single-quantum correlation spectroscopy
KOH	Potassium hydroxide
MALDI	Matrix assisted laser desorption/ionization
MS	Mass spectrometry
NMR	Nuclear magnetic resonance
PBy	*n*-butylpyridinium
PPA	Pollution Prevention Act
PVP	Poly(*N*-vinyl-2-pyrrolidone)
sc-CO_2	Supercritical carbon dioxide
TAML	Tetra-amido macrocyclic ligand

TOF	Turnover frequency
TOF-MS	Time-of-flight mass spectrometry
TON	Turnover number
TRI	Toxics Release Inventory
VOC	Volatile organic compound

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CHAPTER 1 - INTRODUCTION

1.1 Green Chemistry

Chemistry has been essential for the growth of humankind, contributing to areas such as medicine, agriculture, and transportation. However, these amazing accomplishments have not come freely; the manufacturing, use, and disposal of chemicals has greatly affected the environment. Although the chemical industry has its origins in the 19th century, only recently has the issue of chemical substance's impact on the environment been brought into the open. To address these issues, various acts have been established in order to combat the issues hurting the environment. In 1986, under the Emergency Planning and Community Right-to-Know Act, the United States Congress established the Toxics Release Inventory (TRI). Through TRI, a record is kept of the releases of toxic chemicals into the environment on a facility-by-facility basis. Although this provides valuable information, only 689 chemicals and chemical categories are covered, a small fraction of the multitude of substances in commercial use today.[1] For the 2013 reporting year, there were 4.14 billion pounds of hazardous substances released to the environment, the chemical industry being in the top three of industrial sectors responsible for such releases (Figure 1.1). Other countries (e.g. Canada) and regions (e.g. European Union) have similar laws in place.

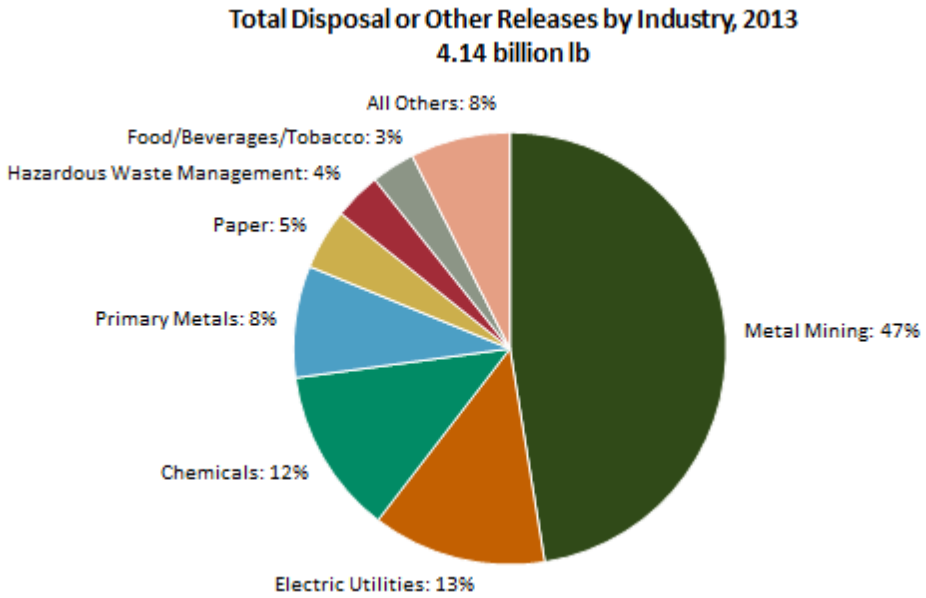

Figure 1.1: Proportion of hazardous waste released to the environment by the major industrial sectors.[2]

In 1990, the Pollution Prevention Act (PPA) was passed by the United States Congress, setting the basis for environmental policies worldwide, as many countries followed their lead in this field. This national environmental policy was set stating that when possible, pollution should be prevented or reduced at the source.[3] With regards to this, chemists are major players in preventing and reducing pollution. For instance, analytical chemists can detect and monitor environmental problems and physical chemists can develop models to simulate environmental phenomena. Additionally, synthetic chemists, those involved in the design and manufacturing of new chemicals, have the choice of being environmentally considerate. Historically, synthetic chemists have been judged to be ignorant of the environment and therefore the ones to be blamed for the release of toxic chemicals into the world.[4] Certainly part of the blame is on industry placing importance on cost efficiency and economic benefits rather than environmental

impacts. However, the advent of various bills and acts regarding the environment has brought additional costs to chemical processes such as waste disposal, liability, and treatment, causing the costs of many syntheses to increase exponentially. Reducing these indirect costs is possible through the redesign of the chemicals and their synthetic routes, specifically through green chemistry.

Green chemistry is a fast, evolving type of pollution prevention that is being more and more integrated into chemist's everyday research. The concept of green chemistry is the use of a set of standards in the design, manufacture, and application of chemicals through the elimination or reduction of hazardous substances. Based on this idea, Anastas and Warner proposed the twelve principles of green chemistry (Figure 1.2)[4] for those wishing to perform chemistry in an environmentally aware manner. These principles are not meant to be strict rules to be followed, but more guidelines in the stride towards improving previous synthetic methods to reduce waste and thereby benefiting the environment.

The twelve principles of green chemistry
1. It is better to prevent waste than to treat or clean up waste after it is formed
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process in the final product
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity
5. The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and, innocuous when used
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material of feedstock should be renewable rather than depleting wherever technically and economically practicable
8. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products
11. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances
12. Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires

Figure 1.2: Twelve principles of green chemistry proposed by Anastas and Warner.[4]

1.1.1 Solvent Replacement and Ionic Liquids

Solvents play a critical role in chemistry: dissolving solids, aiding in mass and heat transfer, influencing viscosity, and assisting in separations and purifications of products. However, traditional solvents are often volatile organic compounds (VOCs), which when paired with the disposal of solvents at the end of reactions, have become a major environmental concern. These VOCs are frequently highly flammable, able to form low-level ozone and smog, and can cause a variety of detrimental health effects such as

headaches and eye irritation. One crucial issue with VOCs is that some are suspected or known carcinogens, such as benzene, an excellent and unreactive solvent.[5] Therefore, with the advent of green chemistry, substituting hazardous solvents with those having benign environmental, health, and safety properties has become a priority.

The ideal solution would be to run reactions solvent-free, as achieved for some of the organic molecules described in Chapter 3 of this thesis, however the majority of chemical syntheses still require solvents. The model solvent would then be easy to recycle, have low toxicity, and will not contaminate the end product. Unfortunately, it is not possible for one solvent to be the be-all and end-all of solvents as different syntheses require different properties from the solvents used. Already many alternative solvents are being investigated and used in a wide range of reactions, such as water, and supercritical fluids.[5]

Ionic liquids are alternative solvents that have been extensively investigated. Also known as room temperature ionic liquids, they are defined as salts with melting points below 100 °C. The great interest in ionic liquids is due to their unique chemical and physical properties such as thermal and chemical stability, selective solubility, and high reusability.[6] For instance, because they have little to no vapour pressure, they are easy to separate from volatile organic products via distillation or vacuum. As well, their thermal stability allows them to be used over a wide temperature range which traditional solvents are not capable of. Most importantly, the properties of ionic liquids can be easily adjusted by changing the anion and cation (Figure 1.3).[5] There are many reviews and books on the subject of ionic liquids: an excellent introduction to ionic liquids has been written by

Michael Freemantle;[6] and the use of ionic liquids in synthesis and catalysis has been extensively reviewed by Hallet and Welton.[7]

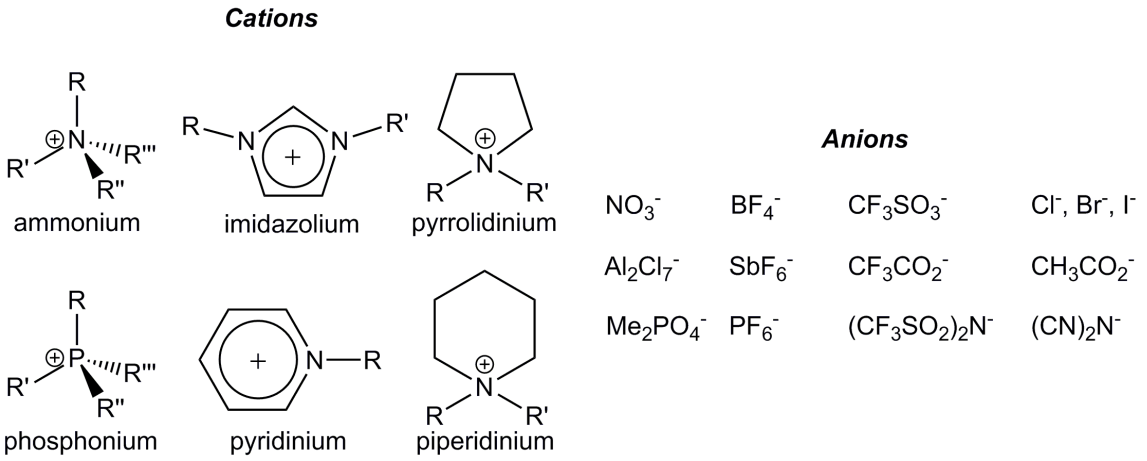

Figure 1.3: Common cations and anions used to produce room temperature ionic liquids.[5]

1.1.2 Alternative Feedstocks and Starting Materials

The starting point in a chemical synthesis is vital in the manufacturing, processing, and application of the end product: if the starting material or feedstock has a negative effect (specifically environmental), it is very likely to produce an overall negative result. Especially in regards to commodity chemicals produced on a large scale, the choice of a certain feedstock can prompt the market in such a way that its primary reason for existing is its role as a feedstock. This means that the choice of what feedstock is used is very important in the decision-making process of green chemistry.

For instance, petroleum feedstocks, such as natural gas or crude oil, are popular for the generation of fuel for transportation, heating, and lighting, as well as the synthesis of a wide variety of carbon-based chemicals and polymers. However, the chemical

components of petroleum (alkenes, alkanes, and arenes), can be thought of as underfunctionalized, as they lack nitrogen or oxygen functional groups. Industrial petrochemical processes therefore seek to selectively activate these feedstocks by the addition of functional groups to transform them into the desired alcohols, carboxylic acids, amines, etc.[8] Generally, the conversion to these organic chemicals requires the oxidation of petroleum. Historically in all chemical syntheses, this oxidation step is one of the most environmentally polluting steps.[4] Therefore, it would be reasonable to reduce the use of petroleum-based products through the use of alternative feedstocks.

Agricultural and biological feedstocks have been investigated as such alternative feedstocks. As many of these are already highly oxygenated, they would be able to replace petroleum feedstocks as there is no need for the polluting oxygenation step.[4] Another interesting feedstock is carbon dioxide; a renewable source of carbon with the advantages of being abundant, economical, and non-toxic.[9]

1.2 Utilization of Carbon Dioxide

Since the industrial age, fossil fuels have been relied upon as the primary source of energy; currently fossil fuels represent 85% of the world's energy source, thereby producing the by-product carbon dioxide.[9,10] Naturally, carbon dioxide is recycled through the carbon cycle, through photosynthesis in plants and the exchange of carbon dioxide between the oceans and atmosphere. However, humans have caused an imbalance in the global carbon cycle, producing an excess of carbon dioxide that cannot be recycled and which is accumulating in the atmosphere.[11] Concerns have started to grow regarding the greenhouse properties of atmospheric carbon dioxide and whether they are heavily

influencing climate change. With the belief that emissions will continue to grow, effort has turned to investigate the possibility of controlling the production of carbon dioxide.[9,10]

Already a variety of technologies have been investigated in controlling the production of carbon dioxide. Perennial energies (e.g. solar and wind power) appear fitting as they are able to produce electric energy that is an ideal substitute for fossil fuels. However their use is dependent on a country's geographic position. Renewable energy, such as biomass, is another replacement, although it has limitations due to its cost, food-energy competitiveness and land use. In regard to large-scale collection of carbon dixoxide, carbon dioxide capture and storage (CCS) is an ideal technology as it disposes of carbon dioxide into natural storage spaces such as spent oil and gas fields, aquifers, and coal beds. Unfortunately, even though a large volume of carbon dioxide would be disposed of, there are a limited number of disposal sites and the procedure itself is expensive and has intensive energy requirements that would in turn produce a large quantity of carbon dioxide.[9,12] Therefore, a broad spectrum of organizations including industry and government are seeking alternatives to CCS, e.g. capture by algae to produce biofuels and fertilizers.

One technology that is being heavily investigated and already being implemented in the energy and chemical industries is the utilization of carbon dioxide.[9] Essentially this technology is adding a value to a waste, by mimicking the carbon cycle, carbon dioxide will be taken from the atmosphere and converts into various compounds. Although this technology will not solve the greenhouse effect, it is still worthwhile to use carbon

dioxide as it is a cheap, non-toxic and abundant source of carbon. The utilization of carbon dioxide can be classified into three categories; enhanced biological utilization, technological utilization, and chemical utilization.

1.2.1 Enhanced Biological Utilization

In nature, the reduction of carbon dioxide occurs in several organisms, under a range of conditions. These organisms convert inorganic carbon (e.g. carbon dioxide) into organic compounds and produce dioxygen, an important aspect for the survival of living organisms. 'Enhanced fixation' has become increasingly investigated in the scientific and technological world, where biomass is produced under 'non-natural photosynthetic conditions'. Essentially, terrestrial or aquatic biomass are grown in the presence of high concentrations in carbon dioxide. This biomass can then be used to produce biofuels, chemicals, food, and animal feedstock. The carbon dioxide that would be emitted during these productions would then be recycled back into the biomass, resulting in an expansion of the natural carbon cycle.[13]

Terrestrial biomass is often referenced in the discussion of biomass, however it has the problem of competing with food crops for land use.[12] This has turned theinvestigation towards aquatic biomass, which has the advantage of the lack of competition for space to grow. Already it has been found that microalgae have a number of benefits over other plant feedstocks: high photosynthetic conversion and a rapid growth cycle.[11] It has been found that certain strains of microalgae are capable of growing in the presence of NO_x and SO_x. Combining this with the high growth rate, these microalgae strains are able to grow and keep up with the continuous flow of flue gases

from point sources.[11,14] Although this is a broad scope, opportunities to use carbon dioxide in other ways will lead to maximum utilization and potentially allow mankind to maintain atmospheric carbon dioxide levels at their current levels.

1.2.2 Technological Utilization

Technological utilization means using carbon dioxide in applications where it is not converted into other chemicals, such as an additive to beverages, enhanced oil recovery, or as a bactericide.[9,12] Although carbon dioxide is not being converted into storable or disposable materials, and often is vented at the end of reactions, the technological utilization is still important in reducing the impact of carbon dioxide on climate change. For instance, carbon dioxide can substitute for environmentally harmful chemicals, such as chlorofluorocarbons used in air conditioners. As well, carbon dioxide can replace chemicals that require high energy for production, or those that when used, produce a great deal of waste.[12]

As a technological fluid, supercritical carbon dioxide (sc-CO_2) is of great interest due to its wide range of varying properties.[5] A supercritical fluid occurs when a substance is held above its critical temperature and pressure, which in the case of carbon dioxide is 31 °C (304 K) and 72.9 atm. Properties such as viscosity and density can be changed by varying the temperature and pressure. As such, sc-CO_2 is capable of acting like a nonpolar organic solvent, such as dichloromethane, and also other more polar solvents (e.g. acetone). Various industrial sectors have started to utilize sc-CO_2 in processes such as decaffeination of coffee beans, catalysis, and nuclear waste treatment. A very important feature of sc-CO_2 is that it is easily recoverable at the end of reactions, and

therefore can be recompressed and re-used. The use of sc-CO_2 dioxide will help control the emission of carbon dioxide as it can be used to replace traditional organic solvents, and there-by prevent the combustion of used solvents at the end of their useful life.[9,12]

1.2.3 Chemical Utilization

Carbon dioxide has only a few applications in the synthesis of chemicals due to its low reactivity. These reactions can be classified into two main categories. (1) Low energy processes, (Figure 1.4, routes A and B) where the entire carbon dioxide molecule is incorporated, there-by producing target molecules of low energy content such as ureas, urethanes and carbamates. Often, energy is contributed by the co-reagent, an electron-rich species such as H_2O, OH^-, or dienes. (2) High energy processes (Figure 1.4, routes C and D) require an input of energy in order to reduce carbon dioxide to other C_1 or C_n molecules. The energy can be conveyed in variety of ways: electrons, metals, hydrogen, heat, or alternative energy sources such as wind.[12]

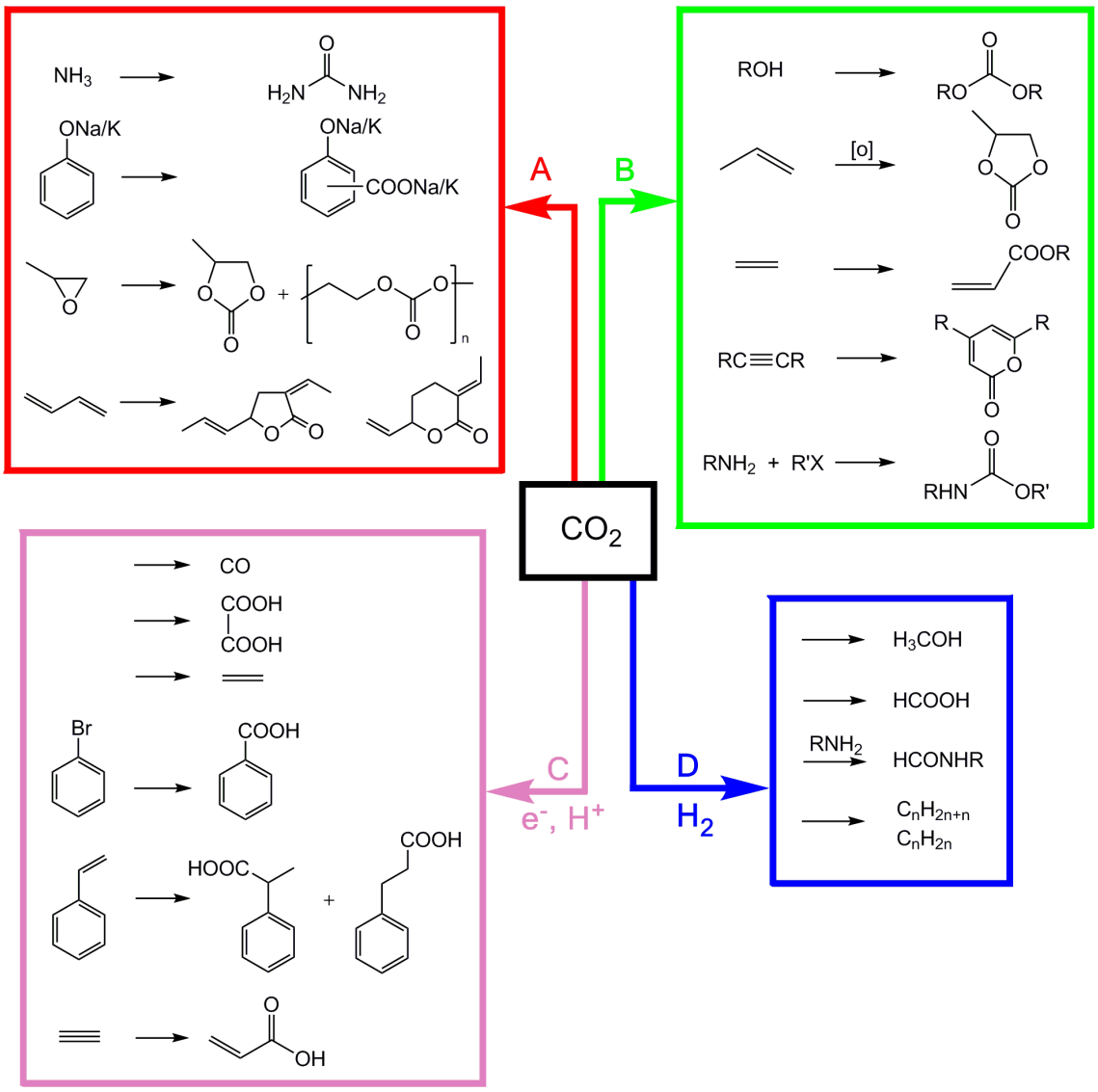

Figure 1.4: Possible applications of carbon dioxide in chemical syntheses.[9]

The above categories can be roughly classified as (1) chemicals and (2) fuels. For the conversion of large volumes of carbon dioxide, the latter has a market size *ca.* 12-14 times larger than that of the former but fuel use would mean that the carbon stored in the molecule would eventually be re-released into the environment.[12]

1.2.3.1 From Carbon Dioxide to Chemicals

Carbon dioxide is able to react with oxygen-containing compounds (e.g. epoxides, alcohols), nitrogen-containing compounds (e.g. ammonia), and unsaturated hydrocarbons (e.g. alkenes, aromatic compounds). The most attractive products from carbon dioxide due to thermodynamics are carbonates, urethanes, and urea because there is no additional reduction step.

Organic carbamates are useful as they play a key role in synthetic chemistry. They act as linkers in combinatorial chemistry, as suitable intermediates for protecting amino-groups, or as the precursors of isocyanates, urea, and polymers. Isocyanates themselves are industrially relevant compounds, often serving as the starting materials for manufacture of dyes, pesticides, resins and plastics, detergents, bleaches, and adhesives. The interest in urea is from their applicability to a wide variety of fields such as petrochemicals, agrochemicals, and pharmaceuticals. However, these useful reagents are often synthesized using the toxic compound phosgene. By using the alternative, cheap and safe carbon dioxide, these opportunities present an appealing and highly environmentally friendly solution for the production of these useful products.[15]

In regards to reducing the emission of carbon dioxide, the chemicals generated from the utilization of carbon dioxide are not needed in large enough quantities to consume the majority of captured carbon dioxide. The conversion of carbon dioxide to energy products is ideal because it will allow for the consumption of more carbon dioxide, as well as provide an alternative to fossil fuels.

1.2.3.2 From Carbon Dioxide to Fuels

Chemical fuels have a high energy density that makes them particularly suitable for storing and transporting energy. Thus carbon dioxide has received a great deal of attention as a reagent for producing chemicals that can store energy chemically. The simplest route in producing energetic compounds is the deoxygenation of carbon dioxide to produce carbon monoxide, through either a thermal or by a radiative route. The reduction of carbon dioxide can be extended beyond this to produce a variety of chemicals according to the conditions and catalysts used (equations (1) - (4)).[12]

$$CO_2 + H_2 \rightarrow CO + H_2O \quad (1)$$

$$CO_2 + H_2 \rightarrow HCOOH \quad (2)$$

$$CO_2 + 3H_2 \rightarrow CH_3OH + H_2O \quad (3)$$

$$CO_2 + 4H_2 \rightarrow CH_4 + 2H_2O \quad (4)$$

These energetic compounds can be designated as solar fuels, which are produced from solar radiation and hold this energy within their chemicals bonds, with protons and electrons as the energy currency. The fuels can be generated through artificial photosynthesis, a light-driven photoelectrochemical reaction, which often requires a suitable catalyst to promote the reaction of photo-generated excited electrons.[16] Through the utilization of carbon dioxide for energetic chemicals, a more convenient and non-fossil carbon-based solar fuel can be produced without changing the current infrastructure (e.g. fuel distribution network).

1.3 Cyclic Carbonates

Since their commercialization in the mid-1950s, cyclic carbonates have become valuable synthetic targets. They are used in a variety of products such as polar solvents, electrolytes for lithium-ion batteries, pharmaceuticals, and raw materials for chemical reactions.[10,17] Specifically five-membered cyclic carbonates such as propylene carbonate or styrene carbonate, are useful alkylating agents for phenols, thiols, and aromatic amines, although these reactions require high temperatures. Industrially, cyclic carbonates are produced from a coupling reaction between carbon dioxide and strained heterocycles, requiring harsh conditions and usually a suitable catalyst. Lewis acid or base catalysts are often used, but require high temperatures and pressures. These conditions become limiting factors with respect to energy and economics.[17] Recently there has been a growing interest in producing cyclic carbonates under more economic conditions, which in turn means a reduction in both cost and emission of carbon dioxide.

1.3.1 Cycloaddition of Carbon Dioxide in Ionic Liquids

Carbon dioxide has low solubility in conventional solvents, which makes it difficult to find the correct solvent for reactions. However, as discussed in section 1.1.1, ionic liquids are able to act as catalysts, reagents, and solvents. They have actually been reported to be one of the most effective media for carbon dioxide fixation in cyclic carbonate synthesis from epoxides.[10,18] Already there have been many publications reporting on the successful use of carbon dioxide in the synthesis of cyclic carbonates. An excellent review written by North, Pasquale, and Young reports on the catalytic conversion of carbon dioxide to produce cyclic carbonates.[17] More recently, the review by

He *et al.* has reported on using ionic liquids as catalysts for the synthesis of cyclic carbonates from carbon dioxide and epoxides.[18]

Peng and Deng were the first to report the successful synthesis of cyclic carbonates using ionic liquids. Using room temperature ionic liquids based on 1-*n*-butyl-3-methylimidazolium (BMIm) and *n*-butylpyridinium (PBy) salts as the catalytic media, they studied the cycloaddition of carbon dioxide with propylene oxide. They determined that the catalytic activity of the ionic liquid was affected by both the cation and anion: the activity decreased in the order of imidazolium > pyridinium, and BF_4^- > Cl^- > PF_6^-. Based on these results, they determined the most active catalyst was [BMIm]BF_4, which gave a TON of 450, and was able to be recycled at least 5 times with only a slight loss in catalytic activit,[19] TON is turnover number and refers to the moles of product produced per mole of catalyst.

The first review that focused on carbon dioxide in cyclic carbonate synthesis using ionic liquid catalyzed reactions was by Arai and co-workers in 2005. They concluded that Lewis acidic compounds of metal halides or metal complexes with little to no activity greatly enhanced the activity of ionic liquids.[20] This phenomenon can be observed in many papers, such as that reported by Wu *et al.,* where they used a catalytic system of $ZnBr_2$ and different phosphonium salts for the solvent-free synthesis of cyclic carbonates. They discovered that the halide ions of the phosphonium salt had an important role in the reaction. When $ZnBr_2$ was paired with phosphine oxide, there was no catalytic activity, but excellent TON was achieved using phosphonium halide salts. Specifically, PPh_4I with

$ZnBr_2$ produced a TON > 6000, with significantly less activity from the Br- and Cl-phosphonium analogues (TON 5800 and 3400 respectively).[21]

Supported ionic liquids have also been investigated, both organic (synthetic polymer, biopolymer) and inorganic (silica, alumina), for their use in cyclic carbonate synthesis. Xie *et al.* reported grafting ionic liquids functionalized with glycidyl groups onto amino and carboxyl functionalized inorganic (SBA15 and silica) and organic (polymer spheres) supports and their use as catalysts. They discovered that the silica supported materials had similar activities to that of the homogeneous glycidyl functionalized ionic liquids. Remarkably, a significantly enhanced reactivity was observed by the organic polymer supported analogues, producing TOF approximately 40 times greater than the homogeneous ionic liquid. TOF is turnover frequency and is calculated by dividing TON by the time that the reaction was performed over, and accordingly has units of $time^{-1}$. Xie *et al.* suggested that the polymer-based catalyst, as it was more easily dispersed in the epoxide, had increased opportunities to interact with the substrate, there-by leading to an increased reaction rate.[22]

Xiao *et al.* reported the synthesis of cyclic carbonate using a chitosan-supported $ZnCl_2$ catalyst in combination with a range of salts. Through the conversion of propylene oxide, they determined the order of reactivity of the ionic co-catalysts was [BMIm]Br > $[Bu_4N]$Br > [BuPy]Br > [BMIm]Cl. Using the optimal ionic co-catalyst, they obtained excellent TOF for propylene carbonate (2717 h^{-1}), styrene carbonate (1454 h^{-1}), and cyclohexene carbonate (532 h^{-1}). A synthetic polymer support, poly(*N*-vinyl-2-pyrrolidone) (PVP), was run and a comparison showed that the biopolymer produced a

higher activity. This was likely due to the hydroxyl residues within the biopolymer interacting with the epoxide, residues which are absent in PVP.[23]

1.3.2 One-Pot Multistep Reactions

Two established methods are shown in Figure 1.5 for the production of cyclic carbonates with carbon dioxide in the presence of ionic liquids. The first method (i) has been highly developed as already discussed above. However, method (ii) is of greater interest, where when starting with the alkene, the required epoxide is formed *in situ* ahead of the subsequent cycloaddition reaction with carbon dioxide. By performing this reaction as a one-pot multistep route, this would allow the synthesis of cyclic carbonates to be safer and potentially reduce costs. The epoxides, which are more toxic and hazardous than alkenes and carbonates, would not require purification and handling. Therefore, this process would produce a more cost-effective product while reducing or eliminating the use of or the formation of by-products, toxic feedstocks, and solvents.

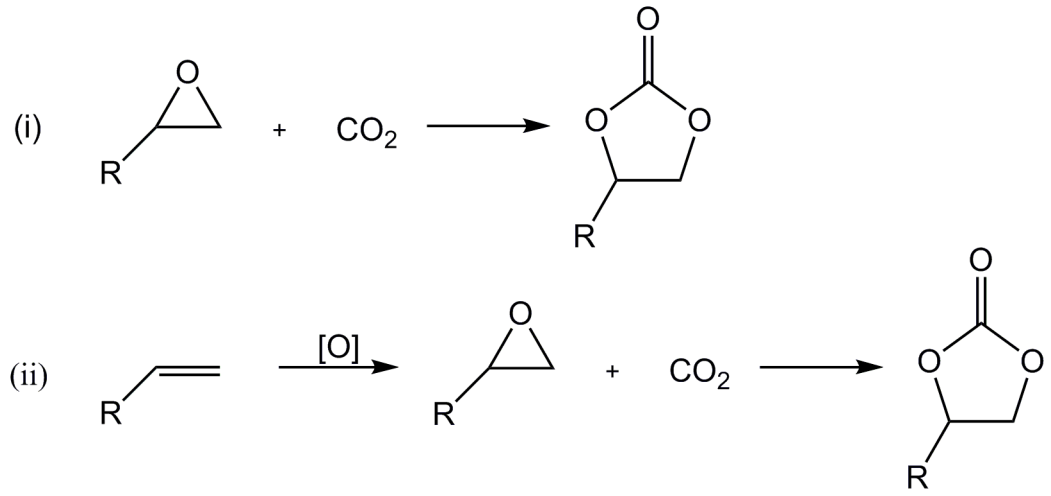

Figure 1.5: General reaction scheme for synthesis of cyclic carbonates with carbon dioxide via (i) cycloaddition of epoxides and (ii) oxidation of alkenes and carboxylation of an intermediate epoxide. [O] = oxidant.

The review by He *et al.* has highlighted reports on the successful one-pot multi-step synthesis of cyclic carbonates from the appropriate olefin.[18] Such as Ono *et al.*, where they described such a process for styrene carbonate, using methyltrioxorhenium as the catalyst and urea hydrogen peroxide as the oxidant for the epoxidation of styrene to styrene oxide. For the carboxylation reaction, a zinc-containing ionic liquid catalyst was used. They determined that in order to obtain a high yield of styrene carbonate, the two steps must be performed at different temperatures. This is because organic peroxides are not stable at high temperatures, but the carboxylation step requires high temperatures.[24] Chen *et al.* used $MoO_2(acac)_2$ with *tert*-butyl hydroperoxide in the oxidation steps and achieved excellent TONs. They were able to obtain varying yields of cyclic carbonates when tetrabutylammoniumbromide was used in the carboxylation step.[25] Recently, Jasiak *et al.* were able to achieve a 60% yield of styrene carbonate through a one-pot synthesis. The epoxidation step involved using anhydrous *tert*-butyl hydroperoxide as the oxidant,

and gold nanoparticles that were immobilized on multi-walled carbon nanotubes as the catalyst. Then the cycloaddition of carbon dioxide with the resulting epoxide was catalyzed using a [BMIm]Br-$ZnBr_2$ system.[26]

Examining these reports and others on one-pot multistep reactions, there is a similarity in the oxidant used in the epoxidation of the alkenes. Often the oxidant that is used is an organic peroxide, such as *tert*-butyl hydroperoxide, or cumene hydroperoxide, which are often flammable and explosive. However, out of the commercially available peroxide reagents, there is one that is considered 'green': hydrogen peroxide, which is cheap and the only by-products are water and oxygen.

Hydrogen peroxide has been reported more widely in the synthesis of epoxides from alkenes. Song *et al.* have had success in the epoxidation of styrene using hydrogen peroxide in ionic liquids in the presence of carbon dioxide and KOH without any metallic catalysts.[27] Ho *et al.* described the epoxidation of lipophilic alkenes using H_2O_2 in ionic liquids under a carbon dioxide saturated environment in the presence of a catalytic amount of Mn(II) salt.[28] Therefore, if the correct metals are present in the ionic liquid, a more atom efficient method of producing epoxides from the alkenes could be found and the epoxides might then be converted directly into carbonates. This is one of the key objectives of the research presented in this thesis i.e. development of a one-pot alkene epoxidation-carboxylation reaction using hydrogen peroxide as the oxidant.

1.4 Design of Catalysts for Epoxidation and Carboxylation Reactions

In place of catalytic ionic liquids, metal catalysts have been used for oxidation and carboxylation reactions, normally in conventional reaction media (i.e. organic solvents). Especially for the synthesis of cyclic carbonates, the use of metal based systems allowed for lower temperatures as well as higher substrate to catalyst ratios than current commercial processes.[29] A survey of the reported catalytic structures revealed great interest in tetradentate ligands that yield a planar coordination geometry such as chelating ligands like the tetra-phenylporphyrin (N_4) pioneered by Inoue[30] and the salen (N_2O_2) systems investigated by G.W. Coates.[31]

One of the most useful families of stable oxidation catalysts are TAML-Fe complexes, which have been developed for the past 20 years by Collins and co-workers (Figure 1.6).[32] The stability of these catalysts has been attributed to not only the macrocyclic nature of the ligand but also its amide backbone. Recently Adolph *et al.* have reported the use of amide-containing ligands in the catalytic formation of cyclic carbonates from carbon dioxide and epoxides.[33] Therefore, these types of ligands when paired with a suitable metal might yield catalysts suitable for one-pot epoxidation-carboxylation reactions such as those described in section 1.3.

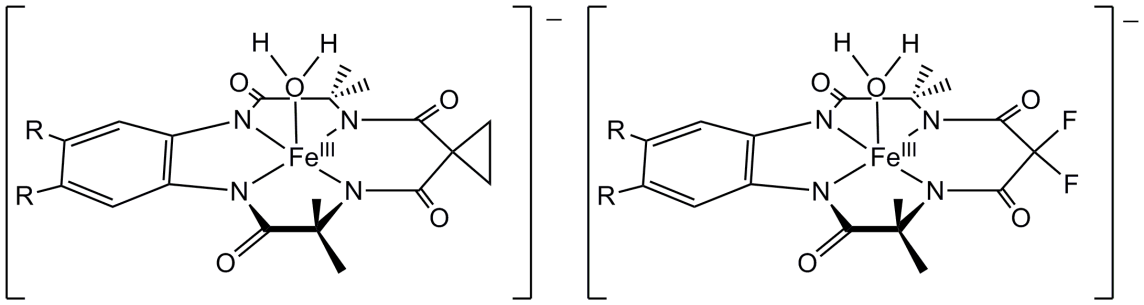

Figure 1.6: TAML-Fe complexes developed by Collins and co-workers.[32]

1.5 Objectives of this Thesis

The synthesis of cyclic carbonates from epoxides has been studied by many scientists and reviewed extensively, but there is growing interest in a one-pot multistep synthesis from alkenes that circumvents the need to isolate the intermediate epoxide. There has been success in using ionic liquids alongside carbon dioxide in such one-pot routes, however the majority of oxidants used are organic peroxides, which are dangerous to handle and potentially harmful to the environment. Metal catalysts have also garnered interest for their application to the synthesis of cyclic carbonates. Thus, the aims of the research described in this thesis are: (a) the design of a one-pot multistep synthesis of cyclic carbonates from the appropriate alkene using carbon dioxide in ionic liquids, alongside a green oxidant; (b) the synthesis of bis(amide) ligands for catalyst development aimed at epoxidation-carboxylation reactions.

In this thesis, chapter 2 provides an overview of the process of designing an epoxidation-carboxylation route to styrene carbonate using carbon dioxide and the ionic liquid, [BMIm]Cl. To achieve a satisfactory outcome for the overall process, the

epoxidation of styrene was first optimized, using the green oxidant hydrogen peroxide. The cycloaddition of carbon dioxide with styrene oxide then followed the epoxidation step using a pressure reactor for the production of styrene carbonate. In Chapter 3, the synthesis and characterization of a series of (bis)amide ligands are described. The use of these ligands in catalyst development is currently ongoing in the Kerton research group.

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CHAPTER 2 - ONE-POT MULTISTEP SYNTHESIS OF CYCLIC CARBONATES

2.1 Introduction

As discussed in Section 1.3 of this thesis, there are many reports on the successful synthesis of cyclic carbonates from epoxides in carbon dioxide (CO_2) and ionic liquids. However, the one-pot multistep synthesis of cyclic carbonates from the appropriate alkene has gained interest due to the possibility of a cheaper and safer route. Some progress has been made towards this goal to date, as described in Section 1.3.2, however the majority of the organic oxidants used for the epoxidation of the alkene have all been organic peroxides, which are flammable and explosive. Therefore, in the current research, the use of hydrogen peroxide as the oxidant has been investigated, as it is cheap and the only by-products are water and oxygen.

Hydrogen peroxide has not been explored extensively in this field to date because it tends to lead to slower oxidation reactions than the organic peroxides. This is because without activation, the hydroxide ion is a poor leaving group. The use of bicarbonate ions to activate hydrogen peroxide has been described, in which sodium bicarbonate is reported to activate hydrogen peroxide into the active species peroxymonocarbonate ion, HCO_4^-.[1] It is well known that carbonic acid and therefore bicarbonate are formed when CO_2 reacts with water. Therefore, the peroxymonocarbonate acid could be formed by the reaction of aqueous hydrogen peroxide and carbon dioxide.

Indeed, the successful epoxidation of alkenes has been reported using a CO_2-H_2O_2-H_2O biphasic system along with an appropriate base at a suitable concentration.

Chan and co-workers reported on the successful epoxidation of alkenes using the peroxymonocarbonate ion generated from a mixture of H_2O_2, NaOH, water, and ambient pressure of carbon dioxide in [BMIm][BF_4] in the presence of a catalytic amount of manganese salt. They determined the importance of the manganese salt, for in its absence, very low yields of epoxides were produced.[2] Song *et al.* also reported on successfully synthesizing styrene oxide using H_2O_2, CO_2, and KOH in various ionic liquids. At 40 °C and 20 bar CO_2, they were able to obtain with [BMIm][BF_4] a 96% conversion and a 69% yield of styrene oxide. In the case of [BMIm]Cl, they produced a 65% conversion and a 34% yield.[3] These reports gave the starting point toward achieving the objectives of this thesis.

2.2 Epoxidation Results

In order to obtain a sufficient outcome for the overall process, the epoxidation step of the one-pot multistep synthesis was optimized first. Various parameters including reaction time, amount and identity of transition metal catalyst were changed in order to determine their effects on the epoxidation of styrene to styrene oxide.

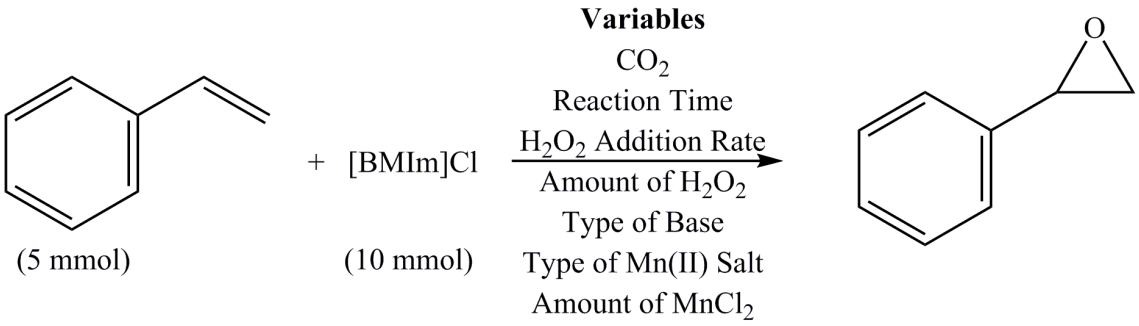

Figure 2.1: Parameters studied in the optimization of the epoxidation of styrene to styrene oxide.

The epoxidation of styrene involved the mixture of [BMIm]Cl, $MnCl_2 \cdot 4\ H_2O$, KOH, water, and styrene in a vial. Aqueous H_2O_2 was added slowly via a syringe and syringe pump while a balloon provided atmospheric pressure of CO_2. A vent was added to prevent the build-up of pressure that might occur due to the decomposition of H_2O_2. After the addition, the reaction was left stirring for 4 hours, after which the CO_2 balloon was removed and the organic layer was extracted with ethyl acetate for analysis by GC-MS. Yields and conversions were determined by GC against an internal standard of dodecane (Appendix 1). Reactions of the same conditions were run three or more times in order to obtain the average and standard deviation of the yield of styrene oxide and the conversion of styrene.

Before the addition of styrene to the vial ([BMIm]Cl, $MnCl_2 \cdot 4\ H_2O$, KOH, and water mixture), it contained a heterogeneous dark brown mixture. Although both KOH and $MnCl_2 \cdot 4\ H_2O$ are soluble in water by themselves, when mixed together they produced a brown precipitate of $Mn(OH)_2$. The addition of styrene produced two layers, with the styrene sitting on the top as it is not soluble in water. During the addition of hydrogen peroxide, with each drop the dark brown mixture became lighter in colour, eventually becoming a tan colour when the addition was finished. There was no colour difference after four hours of stirring.

Based on the results presented below, it was determined that the overall optimum conditions were: KOH (1 mmol); $MnCl_2 \cdot 4\ H_2O$ (0.13 mmol); 4 hours, 30% H_2O_2 (25 mmol) at a rate of 0.1 mL/min, room temperature and 1 atm of CO_2. These conditions led to a 94% conversion of styrene and a 52% yield of styrene oxide.

2.2.1 Oxidation in the Presence and Absence of Carbon Dioxide

Carbon dioxide is reported to activate hydrogen peroxide into a more active oxidizing species, the peroxymonocarbonate ion. In this research, for reactions that were run with carbon dioxide, a colour change was observed during the addition of hydrogen peroxide, with GC-analysis confirming the formation of styrene oxide. In order to confirm that carbon dioxide is a required component in these reactions, one reaction was run in the absence of carbon dioxide. During the addition of hydrogen peroxide, there was no characteristic colour change from brown to tan. Further analysis by GC-MS showed only the presence of styrene, with styrene oxide being absent. Therefore, carbon dioxide is indeed required to activate hydrogen peroxide for the epoxidation of styrene under the conditions explored.

2.2.2 Reaction Time

The effect of reaction time on the conversion of styrene and the yield of styrene oxide are presented in Table 2.1 and Figure 2.2. There is no significant difference over reaction times varying from 30 min to 5 hours based on the standard deviation. Considering that Song *et al*. reported an increase in conversion and product yield over a range of 0-4 hours,[3] this may suggest there are possible significant differences between their catalytic system and that described above. For instance, the aliquots taken to run on the GC-MS are taken from a suspension. As it is not a homogenous mixture, this may not be the most accurate way to view what is in the reaction at a given time. However, an isolated crude yield of styrene oxide was obtained (65%) demonstrating that the GC

values, although from an aliquot of a heterogeneous mixture, are an accurate reflection of the system.

An attempt was made to take aliquots of the same reaction at different times, but it proved to be too difficult. For the first two times (0.5 and 1 hour), no styrene was observed by GC, but in the later times, styrene was found to be present. As sampling the reaction mixture was difficult to do, it was not repeated during the course of this project but it may be worth revisiting by another researcher in the future.

Table 2.1: Effect of reaction time on styrene conversion and styrene oxide yield.

Entry [a]	Reaction time (h)	Conversion (%)	Yield (%) [b]
1	0.5	92.8 ± 6.9	28.6 ± 9.4
2	1	93.1 ± 5.7	33.3 ± 13.1
3	2	91.3 ± 4.3	28.3 ± 12.5
4	3	90.6 ± 8.3	31.1 ± 5.1
5	4	95.5 ± 0.6	35.8 ± 3.4
6	5	95.9 ± 1.4	31.5 ± 5.7

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; [b] Yields determined by GC versus an internal standard of dodecane.

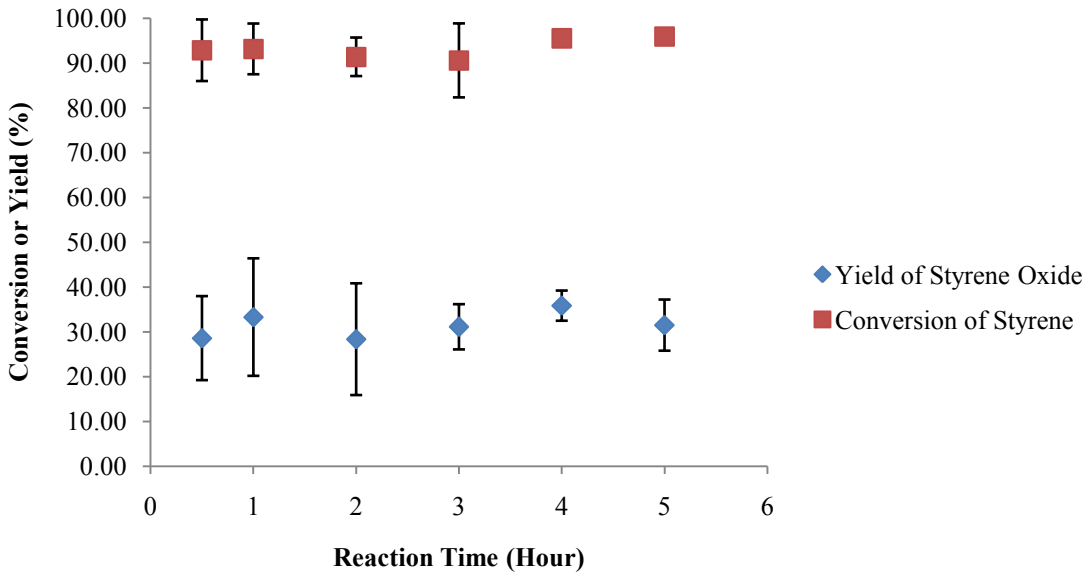

Figure 2.2: Effect of reaction time on the conversion of styrene and the yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4\ H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.3 Addition Rate of Hydrogen Peroxide

The effect of the addition rate of hydrogen peroxide on styrene conversion and styrene oxide yield is presented in Table 2.2 and Figure 2.3. Rapid addition of the oxidizing agent can cause over-oxidation of the product, or in the case of hydrogen peroxide, if added too quickly, it can catalytically decompose prior to reacting with the substrate. There was no significant difference observed for the different addition rates, with the exception of the addition rate of 0.2 mL/min, which had no typical colour change (staying dark brown over time) and no styrene oxide was observed through GC-analysis. It is likely that the rapid addition of H_2O_2 caused either the decomposition of the catalyst system or of the oxidant itself. In future reactions, an addition rate of 0.1 mL/min was used.

Dilution of hydrogen peroxide was attempted to prevent its decomposition by creating a 1:1 ratio of H_2O_2 (25 mmol) and water, and added at a 0.1 mL/min rate. This gave a 34% yield of styrene oxide and 88% conversion of styrene, which does not show any significant difference from previous reactions. As such, dilution was not further pursued.

Table 2.2: Effect of hydrogen peroxide addition time on styrene conversion and yield of styrene oxide.

Entry [a]	Addition Rate (mL/min)	Time (min)	Conversion (%)	Yield (%) [b]
1	0.2	11.5	90.4 ± 0.9	0.0 ± 0.0
2	0.14	17	95.5 ± 0.6	35.8 ± 3.4
3	0.1	23	92.2 ± 2.4	35.1 ± 5.1
4	0.05	46	93.2 ± 4.4	32.6 ± 3.5

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4 H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. [b] Yields determined by GC versus an internal standard of dodecane.

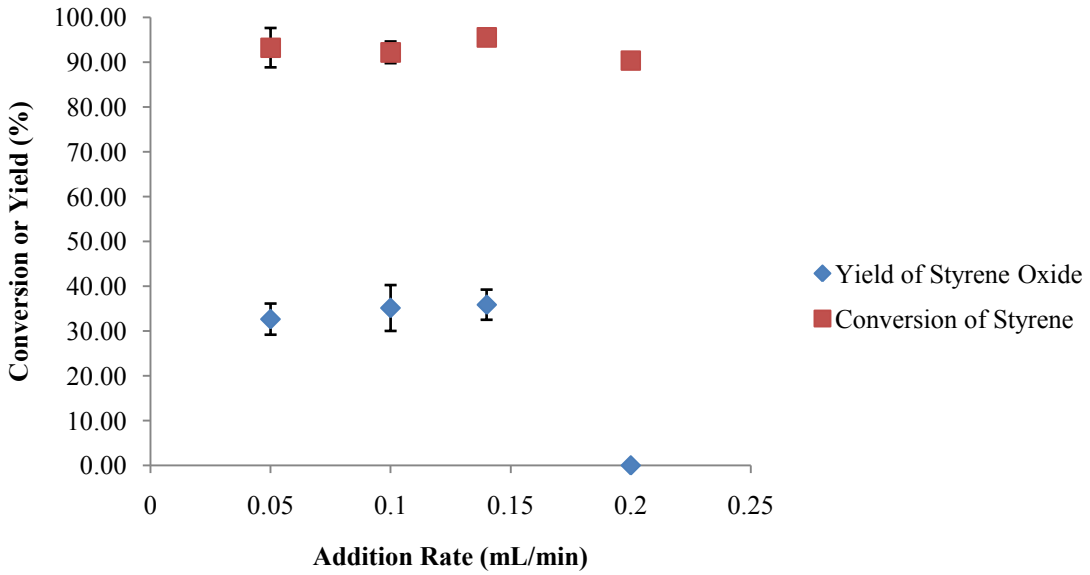

Figure 2.3: Effects of addition rate of hydrogen peroxide on the conversion of styrene and the yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4 H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.4 Amount of Hydrogen Peroxide

The conversion of styrene and yield of styrene oxide are strongly dependent on the equivalents of hydrogen peroxide added as observed in Table 2.3 and Figure 2.4. For every reaction, 5 mmol of styrene was used. A 1:1 ratio of styrene to hydrogen peroxide produced a yield of 5% and a conversion of 80%. With each increase of hydrogen peroxide, an increase in both yield and conversion was observed, with 25 mmol of hydrogen peroxide producing the highest yield at 43% with a 93% conversion. However, a further increase to 30 mmol of H_2O_2 afforded a decrease in the yield of styrene oxide while conversion of styrene stayed the same. It is possible that the presence of large amounts of the oxidant would cause side reactions of the epoxide product e.g. ring-opening to form a diol or oxidation to an aldehyde. However, no by-products were observed to have formed. This mystery is further discussed in Section 2.3.

Table 2.3: Effect of hydrogen peroxide addition time on styrene conversion and yield of styrene oxide.

Entry [a]	Amount (mmol)	Conversion (%)	Yield (%) [b]
1	5	79.7 ± 13.0	4.9 ± 6.9
2	10	81.7 ± 12.4	12.5 ± 9.8
3	15	84.8 ± 5.7	29.6 ± 5.4
4	20	89.5 ± 6.9	33.7 ± 5.7
5	25	92.8 ± 3.0	43.2 ± 7.2
6	30	92.4 ± 6.6	34.1 ± 10.2

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4H_2O$, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. [b] Yields determined by GC versus an internal standard of dodecane.

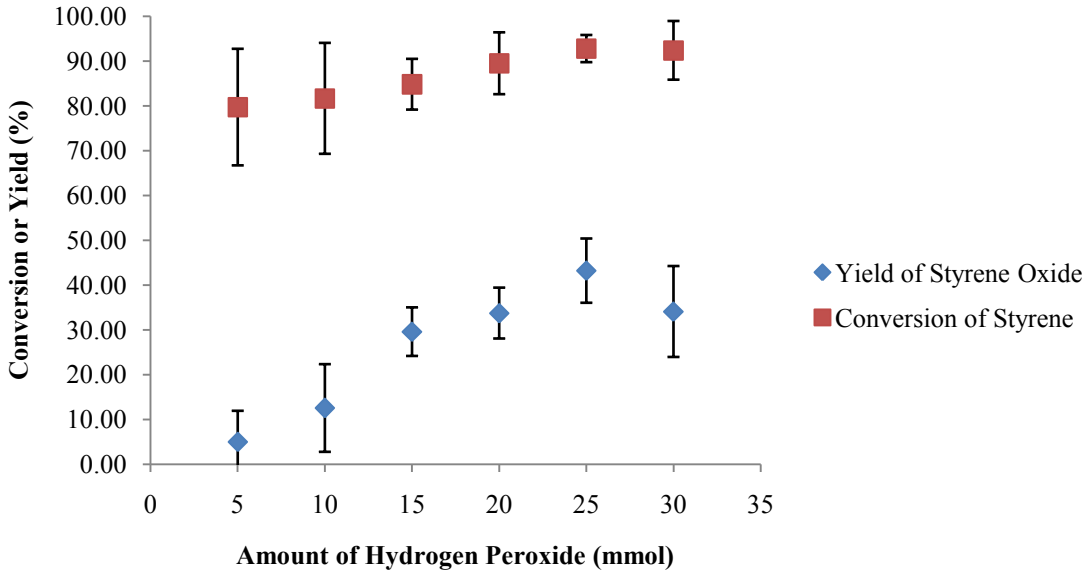

Figure 2.4: Effects of the quantity of hydrogen peroxide on the conversion of styrene and the yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol $MnCl_2 \cdot 4\ H_2O$, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.5 Type of Base Used

It has been reported that epoxidation using the peroxymonocarbonate ion is strongly affected by the pH of the system, and basic conditions were found to be more favourable in such reactions.[1] Potassium hydroxide was used by Song *et al.* because they determined that KOH helped promote the formation of the peroxymonocarbonate ion.[3] Indeed in the current research, a reaction run in the absence of KOH did not produce any styrene oxide, indicating the importance of the base in promoting the formation of the active species.

The effect of sodium bicarbonate and aqueous ammonia as the base were examined, with the results presented in Table 2.4 and Figure 2.5. Aqueous ammonium

hydroxide produced low yields of styrene oxide compared to that of potassium hydroxide. The origin of this difference may be the difference in strength of the two bases (ammonia is a weak base and potassium hydroxide a strong base) but further investigations would be needed to confirm this. Taking standard deviation into account, there is no significant different between the yields using sodium bicarbonate and potassium hydroxide. However, the high standard deviation observed using sodium bicarbonate may be due to the bicarbonate ion competing with carbon dioxide in activating hydrogen peroxide. As such, potassium hydroxide was used as the base in future reactions.

Table 2.4: Effect of different bases used on styrene conversion and yield of styrene oxide.

Entry [a]	Base	Conversion (%)	Yield (%) [b]
1	KOH	92.5 ± 3.5	45.4 ± 5.9
2	$NaHCO_3$	86.5 ± 7.7	36.7 ± 14.9
3	NH_4OH	93.4 ± 3.4	26.6 ± 4.6

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol base, 0.13 mmol $MnCl_2 \cdot 4H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. [b] Yields determined by GC versus an internal standard of dodecane.

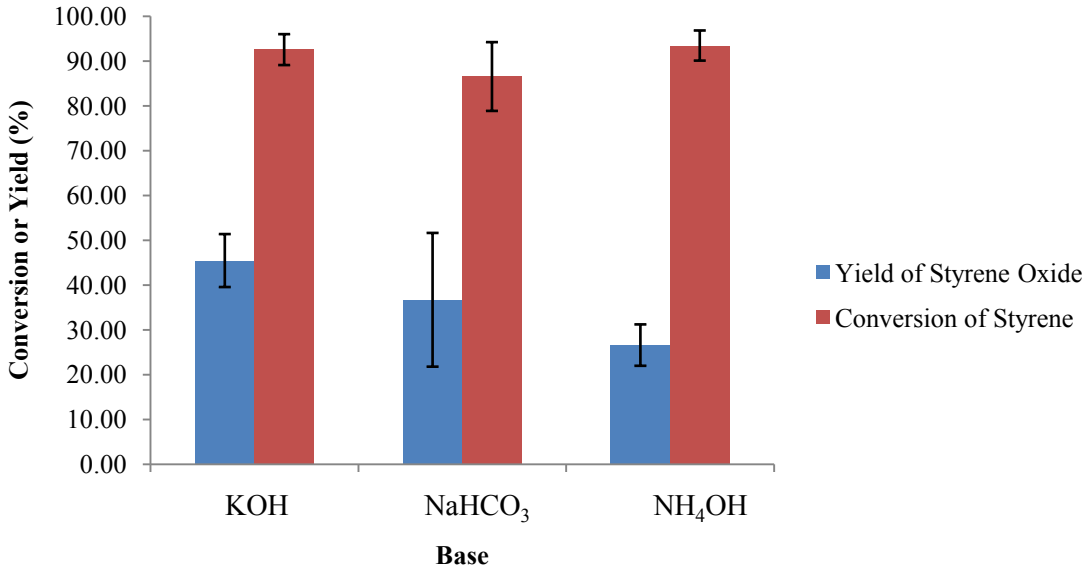

Figure 2.5: Various bases and their effects on the conversion of styrene and yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol base, 0.13 mmol $MnCl_2 \cdot 4 H_2O$, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.6 Type of Mn(II) Salt Used

The different types of Mn(II) salt studied were shown (Table 2.5 and Figure 2.6) to have no effect on the yield of styrene oxide and the conversion of styrene. These results are similar to those reported by Lane *et al.*, where they observed a negligible difference in the epoxidation reaction when using various Mn(II) salts.[4] However, it can be observed that the standard deviations in the GC yields of styrene oxide using of $MnSO_4$ and $Mn(OAc)_2$ are considerably larger than those obtained using $MnCl_2$. It is possible that the anion of these salts is affecting the reaction in such a way to cause these variances. It was decided to continue using $MnCl_2$ as the anion would match the one within the ionic liquid ([BMIm]Cl).

Table 2.5: Effect of different Mn(II) salts used on styrene conversion and yield of styrene oxide.

Entry [a]	Mn(II) Salt	Conversion (%)	Yield (%) [b]
1	$MnCl_2$	92.5 ± 3.5	45.4 ± 5.9
2	$MnSO_4$	93.2 ± 2.2	31.5 ± 15.0
3	$Mn(OAc)_2$	90.7 ± 5.5	30.8 ± 16.1

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol Mn(II), 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. [b] Yields determined by GC versus an internal standard of dodecane.

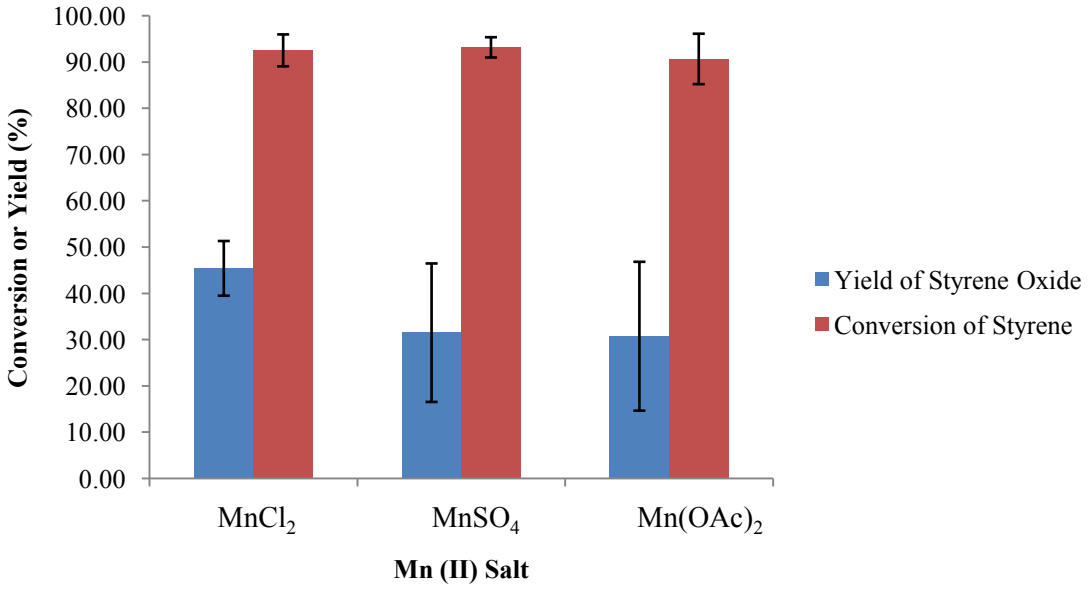

Figure 2.6: Various Mn(II) salts and their effect on the conversion of styrene and yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 0.13 mmol Mn(II), 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.7 Amount of $MnCl_2 \cdot 4\ H_2O$

The amount of $MnCl_2 \cdot 4\ H_2O$ salt used has a significant effect on the conversion of styrene and styrene oxide yield as shown in Table 2.6 and Figure 2.7. It can be observed that with no $MnCl_2 \cdot 4\ H_2O$ present, no styrene oxide was produced. It has been hypothesized that Mn(II) interacts with the peroxymonocarbonate ion in such a way to

cause epoxidation, however the mechanism is still being investigated.[4,5] It was determined that 0.13 mmol (or ~2.5 mol%) was the optimal amount of $MnCl_2 \cdot 4\ H_2O$ to convert 5 mmol of styrene. The decrease in both the yield and the conversion with the increase in $MnCl_2 \cdot 4\ H_2O$ does not have a definite explanation at this time but may be due to over-oxidation or decomposition of the styrene oxide.

Table 2.6: Effect of the amount of $MnCl_2 \cdot 4\ H_2O$ on styrene conversion and the styrene oxide yield.

Entry [a]	$MnCl_2$ Amount (mmol)	Conversion (%)	Yield (%) [b]
1	0.0	39.4 ± 0.0	0.0 ± 0.0
2	0.07	94.4 ± 1.0	33.4 ± 4.0
3	0.13	95.5 ± 0.6	35.8 ± 3.4
4	0.20	91.5 ± 7.4	30.3 ± 3.0
5	0.26	86.6 ± 3.9	18.1 ± 6.3

[a] *Conditions:* 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. [b] Yields determined by GC versus an internal standard of dodecane.

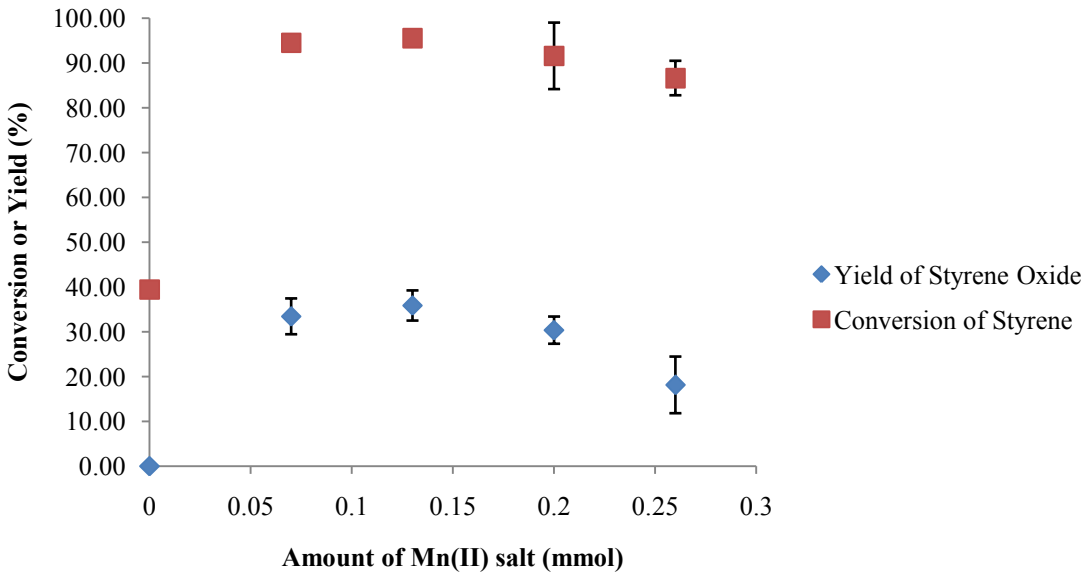

Figure 2.7: Effects of amount of $MnCl_2 \cdot 4\ H_2O$ salt (mmol) relative to styrene on the conversion of styrene and the yield of styrene oxide. 10 mmol [BMIm]Cl, 5 mmol styrene, 1 mmol KOH, 20 mmol H_2O_2, CO_2 Pressure = 1 atm; Temperature = 25 °C; Reaction time = 4 hours. Data obtained from GC analysis on reactions performed in triplicate or more.

2.2.8 Other Co-Catalysts

In preparation for the next step, other metal catalysts that showed promising results in the carboxylation of styrene oxide into styrene carbonate were investigated as potential co-catalysts in the epoxidation of styrene.

The first co-catalyst to be investigated was $ZnBr_2$, as Sun *et al.* were able to achieve a 93% yield of styrene carbonate in [BMIm]Cl, at 140 bar, 80 °C in 1 hour.[6] For the epoxidation step, the use of $ZnBr_2$ was investigated by itself and along with $MnCl_2$. In the reaction with $MnCl_2$, there were various colour changes, with the final mixture being heterogenous, a green brown bottom layer and a colourless top layer. The reaction mixture containing just $ZnBr_2$ stayed a white colour, even after the addition of hydrogen peroxide. Both reactions showed no production of styrene oxide and therefore were not continued into the next step of the synthesis. However, it seems that $ZnBr_2$ somehow inhibits the catalytic epoxidation reaction.

A previous Kerton group student, Qing He, had promising results using Co(II) for carboxylation of styrene oxide where he obtained a 96% yield of styrene carbonate, using choline chloride (ChCl) and $CoCl_2$ at 10 bar, 160 °C and 4 hours.[7] In the current research, a reaction was run with just $CoCl_2$, and the resulting reaction mixtures underwent various colour changes. A dark purple mixture became dark green upon addition of hydrogen peroxide. However, no styrene oxide was observed via GC, so the use of $CoCl_2$ was not continued.

2.2.9 Recycling Studies of [BMIm]Cl

Recycling studies of the ionic liquid phase, which should still contain the catalyst, were attempted. After the organic layer was extracted, the aqueous layer was put under vacuum to remove any residual solvent. Afterwards, more styrene and hydrogen peroxide were added to the aqueous layer (containing ionic liquid, base, and manganese salt). However, there was no characteristic colour change and GC analysis showed no presence of styrene oxide. It is possible that fresh manganese(II) and/or potassium hydroxide is required for the reaction to proceed.

The recovery of just the ionic liquid [BMIm]Cl was attempted. Materials produced from a number of reactions were combined, the organic layer was extracted, and then the aqueous layer was placed under vacuum to remove excess ethyl acetate. Activated charcoal was added and the aqueous mixture was filtered, producing a clear, yellow filtrate. Unfortunately, pure [BMIm]Cl could not be isolated from this solution.

2.3 Styrene Quantitation

2.3.1 GC-MS Calibration Curve

A calibration curve was produced for GC analysis of the styrene conversion and styrene oxide yields (Agilent 5975C VLMSD with Triple-Axis detector), using dodecane as the internal standard (Appendix 2). Analysis of the data showed that the conversion of styrene was very high, but not consistent with the yields of styrene oxide. As previously discussed, there was no evidence of by-products in the chromatographs that would

explain these lower than expected yields. This led to the investigation of other quantitation methods through NMR spectroscopy by use of internal standards.

2.3.2 NMR Quantitation

In order to determine if GC analysis was over-estimating the level of styrene conversion in the reactions (e.g. if the styrene was reacting within the GC inlet via thermal polymerization), various internal standards were investigated to quantify styrene by ^{1}H NMR spectroscopy. Attempts at using acetophenone or 1-methylnapthalene as the internal standard in acetone-d_6 were thwarted as the peaks could not be accurately integrated due to overlap by other peaks. Toluene in DMSO-d_6 allowed for accurate integrations, but when applied to actual reactions, yields > 100% of styrene oxide were obtained, which clearly did not match the original yields from GC analysis. Finally, a method using TMS in $CDCl_3$ as outlined by Zhang *et al.* was attempted,[8] however, trying to concentrate the final mixture ended up with the styrene oxide being removed along with the organic solvent. As such, quantitation by NMR spectroscopy did not seem possible and did not provide any information on the difference between the high conversions of styrene and the moderate yields of styrene oxide observed via GC-MS analyses.

2.3.3 Possible By-Products

Following the failings of the NMR-based quantitation methods, investigation returned to the possibility of by-products. In the epoxidation of styrene, benzaldehyde and phenylacetaldehyde are both possible by-products, but neither were detected in either the

GC or NMR spectra of reaction mixtures. However, due to the oxidizing environment it is possible that the by-products were further oxidized. In the case of benzaldehyde, it could be further oxidized into benzoic acid and then, due to the presence of potassium hydroxide, form potassium benzoate, a water soluble compound (Figure 2.8). As only the organic layer was used in the GC analysis, these compounds would not be observed as they would be removed during sample preparation. To prove this hypothesis, the aqueous layer was acidified with hydrochloric acid in order to generate benzoic acid. A ^{1}H NMR spectrum of the resulting solution showed peaks that could potentially be assigned to benzoic acid, and this was further confirmed with the addition of benzoic acid to the NMR tube and the assigned peaks grew in intensity. Therefore, it is possible to conclude that the difference in styrene oxide yield and styrene conversion is due to over-oxidation of the styrene to yield benzoic acid over the course of the reaction.

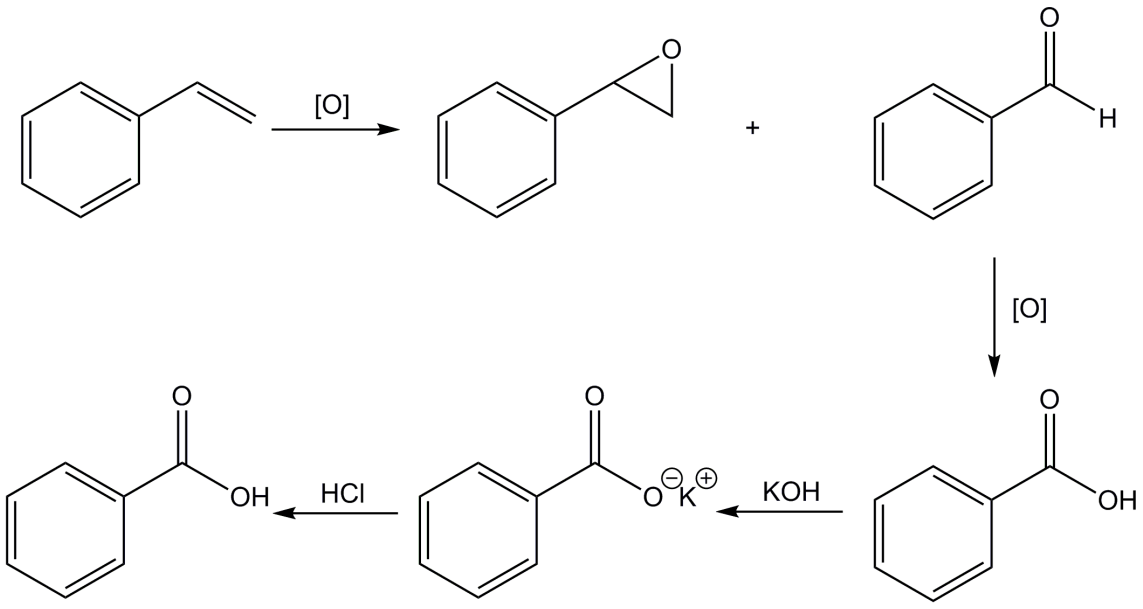

Figure 2.8: Over-oxidation of styrene oxide to produce by-product benzoic acid, and resulting deprotonation to yield water-soluble benzoate (not visible in original GC-MS analyses).

2.4 Epoxidation of Other Alkenes

The epoxidation of other alkenes was attempted in order to determine if this catalytic system was suitable for those other than styrene. The alkenes chosen were based on those that were available in the laboratory (Figure 2.9). Reactions used the optimal conditions determined for the epoxidation of styrene, using 5 mmol of the appropriate alkene.

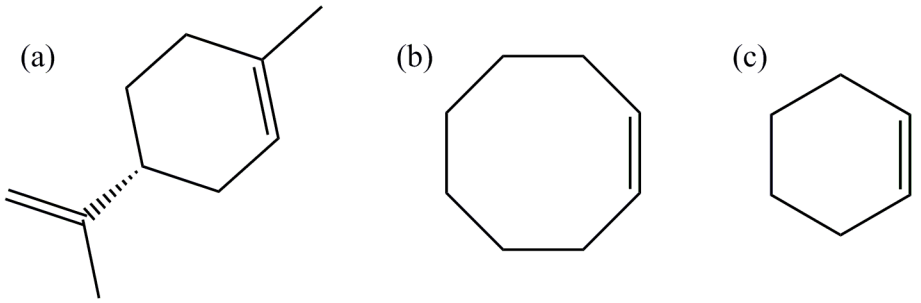

Figure 2.9: (R)-(+)-limonene (a); cyclooctene (b); cyclohexene (c).

2.4.1 (R)-(+)-Limonene

The epoxidation of (R)-(+)-limonene to (R)-(+)-limonene oxide was determined to be successful as the desired product was observed in the GC analysis (Figure 2.10). However, if this reaction was to be further pursued it would require optimization as the amount of starting material present in the GC was very large compared to the amount of product, also various by-products were observed and so this reaction requires further investigation.

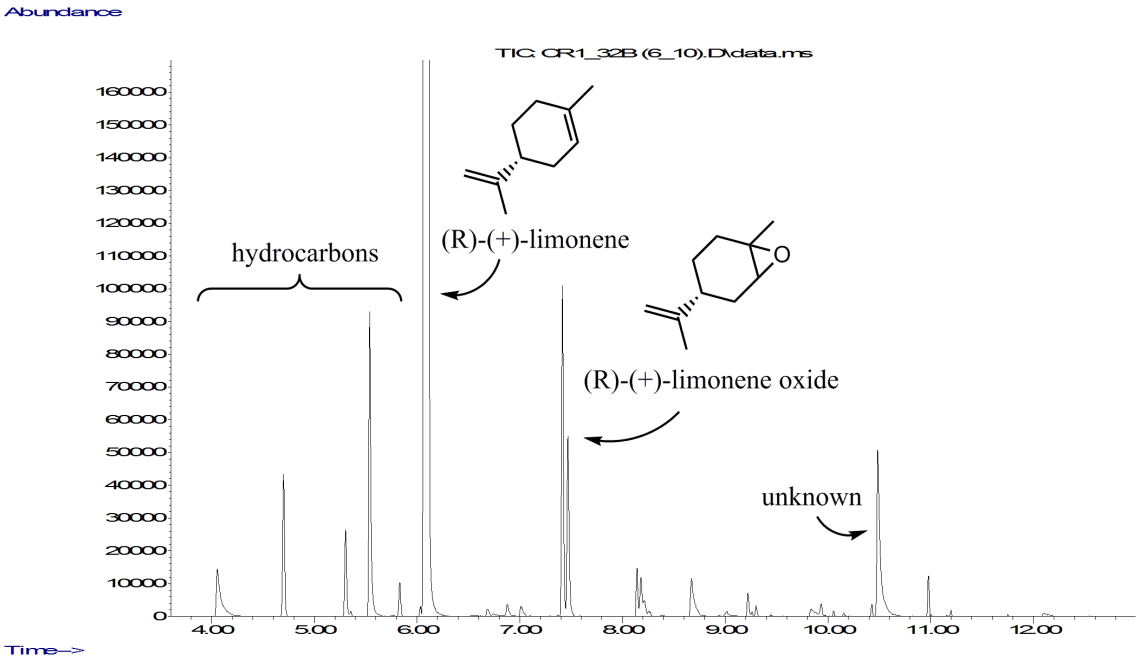

Figure 2.10: Chromatogram of the epoxidation of (R)-(+)-Limonene.

2.4.2 Cyclooctene

Cyclooctene oxide was successfully synthesized from the epoxidation of cyclooctene as shown by GC analysis (Figure 2.11). The presence of 2-octene was also observed, so again further investigation towards reaction optimization would be required if this was further pursued.

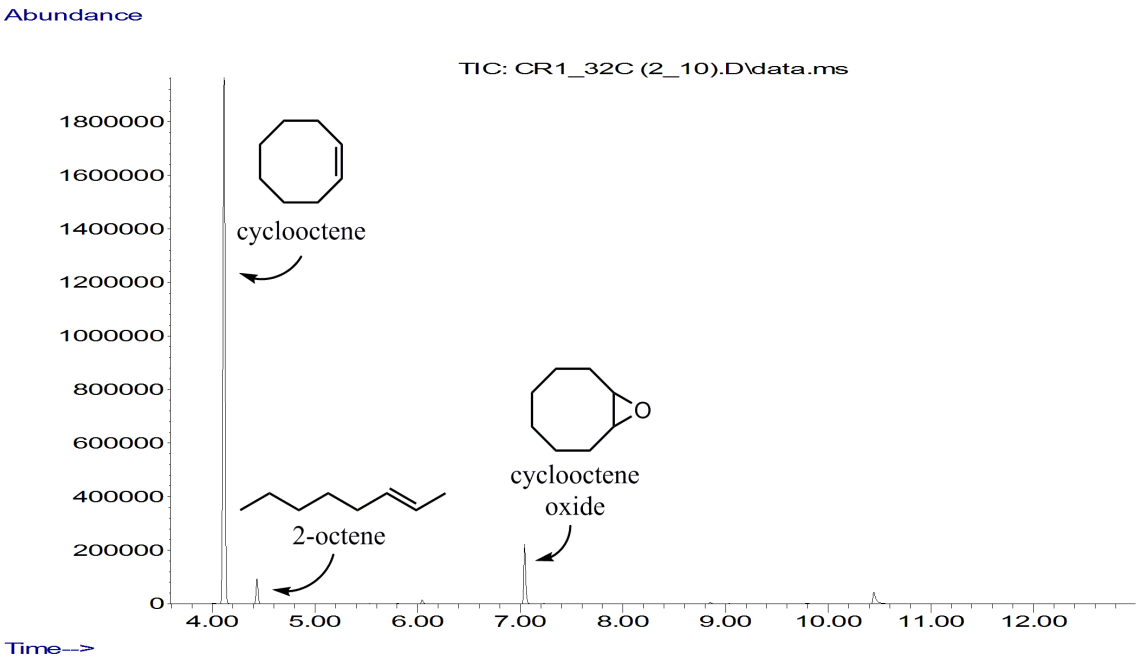

Figure 2.11: Chromatogram of epoxidation of cyclooctene.

2.4.3 Cyclohexene

The epoxidation of cyclohexene did not produce any cyclohexene oxide, as there was no product observed in GC analysis. This may be due to the high stability of cyclohexene preventing the epoxidation of the alkene, and therefore may require higher temperatures in order to activate the double bond.

2.5 Carboxylation Step - Conversion of Styrene Oxide to Styrene Carbonate

The second step was initially attempted at room temperature under and atmosphere of CO_2 but no carbonate was observed. Therefore higher pressure of CO_2 were explored by use of a pressure reactor. An epoxidation mixture was obtained using the optimal parameters described above, and then placed into a 300 mL pressure reactor at 24 bar CO_2 and heated to 80 °C. After 4.5 h, the resulting mixture was extracted and

GC-analysis showed the presence of styrene carbonate, and there was no evidence of styrene or styrene oxide (Figure 2.12). Isolation of styrene carbonate gave a crude yield of 17% based on the initial amount of styrene. This corresponds to a 43% yield based on styrene oxide, which it is assumed was obtained in a 52% yield in the first step.

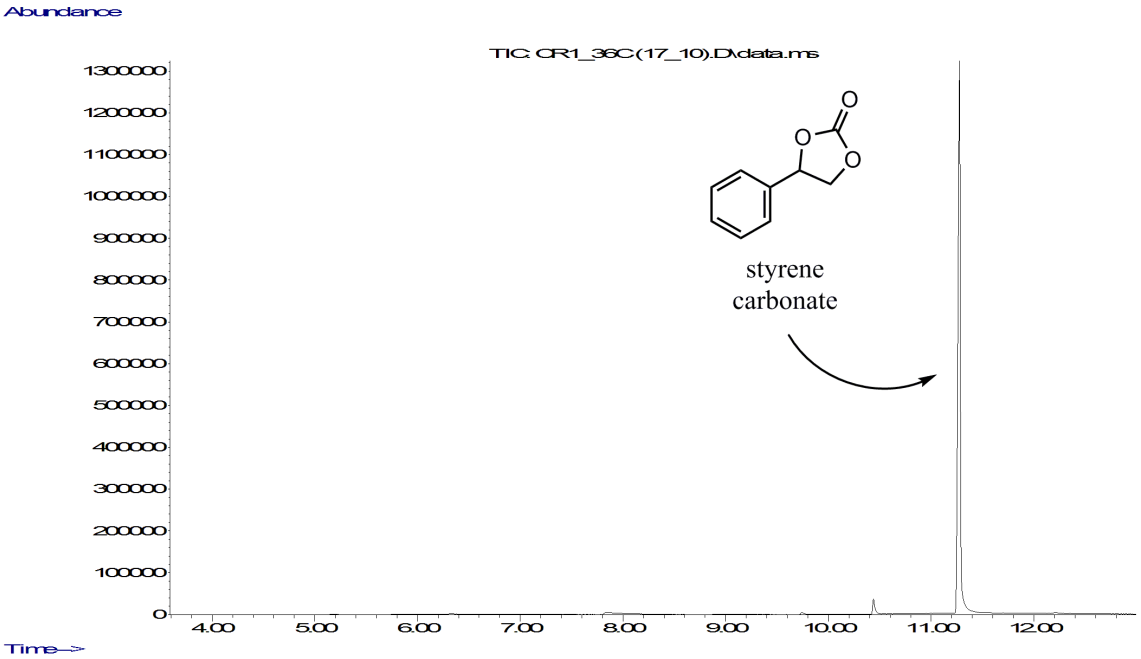

Figure 2.12: Chromatogram of styrene carbonate, retention time: 11.271 min.

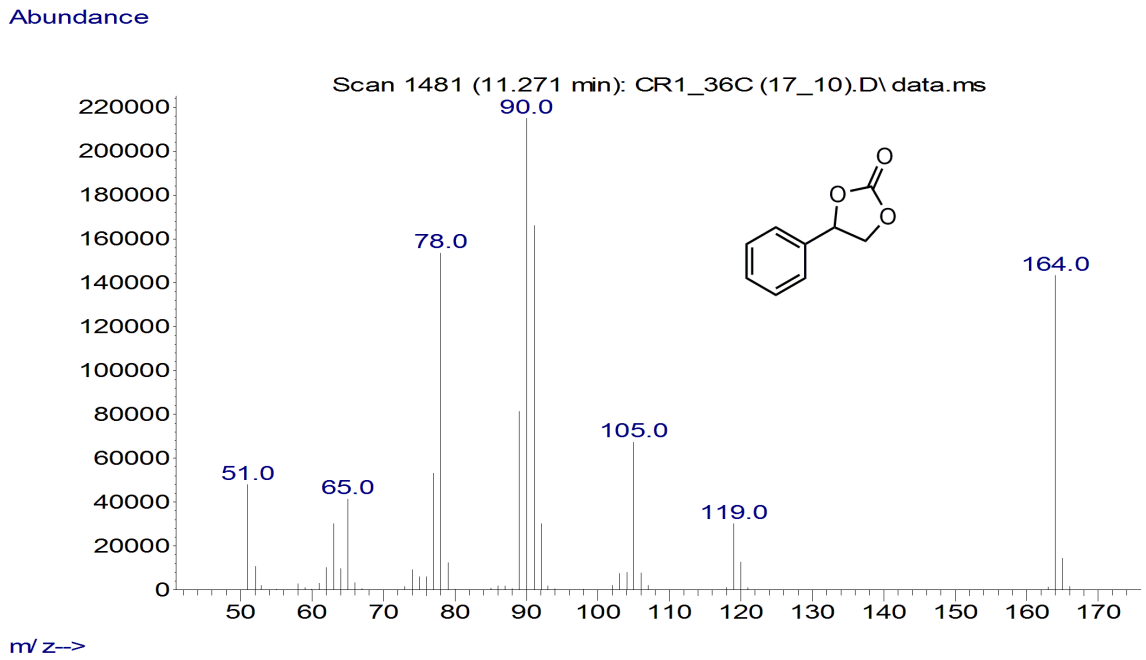

Figure 2.13: Mass spectrum (EI-MS) of styrene carbonate.

In the epoxidation of styrene to styrene oxide, room temperature and atmospheric pressure of carbon dioxide were sufficient for that reaction to proceed. In the synthesis of cyclic carbonates, higher temperatures are required. As already discussed, styrene carbonate was successfully produced at both a high temperature and a higher pressure using a pressure vessel. However, it is possible that only temperature needs to be increased and atmospheric pressure of carbon dioxide is adequate for the cycloaddition reaction to proceed. In order to observe the effects of increased temperature with an atmospheric pressure of carbon dioxide for the cycloaddition of CO_2 to styrene oxide, a reflux apparatus was set up using a Schlenk line connected to a cylinder of carbon dioxide. Two reactions were performed. The first was setup so that the addition of hydrogen peroxide occurred in the same flask. After the addition was finished, the

temperature was increased to 80 °C for 4 hours. The second attempt had the epoxidation step run separately, and the next day the mixture was refluxed at 80 °C for 4 hours. Both attempts showed through GC-MS analysis that styrene carbonate was produced, but yields were not calculated (chromatograms are available in Appendix 3). However the analysis of the first attempt showed the presence of styrene, whereas styrene was absent in the second attempt. This may be due to the reflux being initiated immediately instead of waiting for the typical 4 hour reaction time.

Further investigation toward the optimization of the carboxylation step would be ideal. Parameters such as temperature and length of reaction should be considered. As well, even though atmospheric pressure was determined suitable, various pressures should be explored to obtain a more optimal yield of styrene carbonate. Further studies were not performed as research would also be needed to reduce over-oxidation of the styrene in the initial step too in order to achieve higher overall yields of styrene carbonate.

2.6 Conclusions

The development of a one-pot multistep synthesis of cyclic carbonates from the appropriate alkene using carbon dioxide and ionic liquids was a success, and styrene carbonate could be isolated in a yield of 17% based on styrene. Optimization of the epoxidation of styrene to styrene oxide was needed to ensure a sufficient outcome for the overall process. As such, the optimal conditions were determined to be: KOH (1 mmol); $MnCl_2 \cdot 4\ H_2O$ (0.13 mmol); 4 hours, H_2O_2 (25 mmol) at a rate of 0.1 mL/min, room temperature and 1 atm of CO_2. Under these conditions, a 52% yield of styrene oxide and a 94% conversion of styrene were determined through GC-MS analysis. The discrepancy

between the yield of styrene oxide and the conversion of styrene was determined to be due to over oxidation of the product, there-by generating aqueous by-products. The carboxylation step involved the use of a pressure reactor and an epoxidation mixture created using the optimal parameters. Through GC-MS analysis, the end product was determined to be styrene carbonate, and an isolated 17% yield was obtained.

In the future, although the epoxidation of alkenes other than styrene was attempted, it would be interesting to see the different parameters needed for the epoxidation of different alkenes compared to styrene. As well as continue to the next step, the carboxylation of the intermediate epoxides to their respective cyclic carbonate. One parameter that was not investigated in this thesis, but may have potential, is using different ionic liquids. The choice of [BMIm]Cl was based on its availability, and its ability to produce an acceptable yield of styrene oxide.[3] However, seeing how a different ionic liquid, such as [BMIm]BF_4, would affect the yield and conversion would be interesting to investigate further.

2.7 Experimental

2.7.1 Materials

Styrene, styrene oxide, $MnSO_4$, dodecane, acetophenone, and 1-methylnapthalene were obtained from Sigma-Aldrich. [BMIm]Cl, $ZnBr_2$, (R)-(+)-limonene, and cyclooctene were obtained from Alfa Aesar. KOH, H_2O_2, $NaHCO_3$, $MgSO_4$ and various solvents were obtained from ACP Chemical Inc. Deuterated solvents were purchased from Cambridge Isotope Laboratory Inc. Ammonium hydroxide, $CoCl_2$, $MnCl_2 \cdot 4\ H_2O$,

$Mn(OAc)_2$ and cyclohexene were ordered from Fischer Scientific, J.T. Baker Chemical Co., and BDH Chemicals respectively. CO_2 was obtained from Praxair.

2.7.2 General Procedure for Epoxidation Reactions

In a scintillation vial was placed [BMIm]Cl (10 mmol), $MnCl_2 \cdot 4\ H_2O$ (0.1 mmol), KOH (1 mmol), water (2 mL), and styrene (5 mmol). The vial was capped with a rubber septum, through which a balloon filled with CO_2 and a vent needle were inserted. Hydrogen peroxide (20 mmol) was added slowly via syringe pump (0.1 mL/min). After the addition, the reaction was left to stir with the balloon for 4 hours. An aliquot (0.1 g) of the reaction mixture was extracted with ethyl acetate (3 × 3 mL). The organic layer was then washed with a saturated brine solution (5 mL) and then dried over magnesium sulfate. The extracted mixture was analyzed by GC-MS (Agilent 5975C VLMSD) with Triple-Axis detector. The yield of styrene oxide was determined by GC using dodecane as an internal standard, added right before extraction. Parameters were changed as noted.

Optimum conditions were determined to be: KOH (1 mmol); $MnCl_2 \cdot 4\ H_2O$ (0.13 mmol); 4 hours, H_2O_2 (25 mmol) at a rate of 0.1 mL/min, room temperature and 1 atm of CO_2. Using these conditions, an isolated 65% crude yield was determined for styrene oxide. Further GC-MS analysis showed a 94% conversion of styrene and a 52% yield of styrene oxide.

2.7.3 General Procedure for Carboxylation Reactions

The reaction mixture from 2.7.2 was placed into a 300 mL pressure reactor, and heated to 80 °C and pressurized to 24 bar of CO_2. After 4.5 hours, the reaction was

stopped. The reaction mixture was extracted with ethyl acetate (4 × 10 mL). The organic layer was then washed with a saturated brine solution (15 mL) and dried over magnesium sulfate. The extracted mixture was analyzed by GC-MS (Agilent 5975C VLMSD) with Triple-Axis detector.

2.8 References

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CHAPTER 3 - SYNTHESIS AND CHARACTERIZATION OF BIS(AMIDE)S AS POTENTIAL LIGANDS FOR OXIDATION CATALYSTS

3.1 Introduction

Along with ionic liquid catalysts being used for the synthesis of cyclic carbonates, there has been great interest in metal based systems. The use of metal catalysts would allow for syntheses done at lower temperatures, and/or higher substrate to catalyst ratios than current commercial processes.[1] As already stated in Chapter 1, section 1.4, one of the most useful families of stable oxidation catalysts are the TAML-Fe systems, developed by Collins and co-workers. The stability of these catalysts has been attributed to the amide backbone as well as the macrocylic nature of the ligand.[2] These ideas, along with the recent report by Adolph *et al.* of the use of amide-containing ligands for the catalytic formation of cyclic carbonates from carbon dioxide and epoxides,[3] has provided for the research described in this chapter, namely the synthesis of (bis)amide compounds as possible ligands for new metal catalysts for the production of cyclic carbonates from alkene starting materials.

A starting point for the research described in this chapter was provided by two papers reporting on the synthesis and coordination chemistry of *N,N′*-bis[(2-pyridylmethyl)]propanediamide (**papH$_2$**) (Figure 3.1). It was first reported by Comba *et al.*, whose goal was to develop a ligand with the following properties: (a) the ability to form relatively stable complexes with Co(II), Ni(II), Cu(II), and Zn(II); (b) the ability to undergo substitution of the ligand backbone that would lead to a predictable coordination geometry and tunable metal-ion selectivity; (c) to provide derivatives with similar

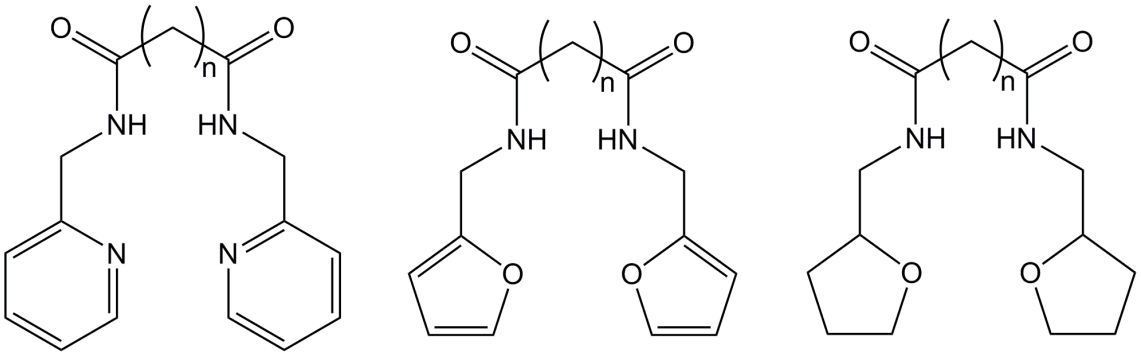
complexation behaviour for metal ion extractions into organic phases and which could be effectively analyzed in aqueous solution. They found **$papH_2$** to posses the desired properties.[4]

Along with the synthesis of **$papH_2$**, they were successful in its coordination to Cu(II) and Ni(II). Structural studies using X-ray analyses of the metal-free **$papH_2$** ligand and the corresponding Cu(II) and Ni(II) complexes showed that the metal-free ligand and the coordinated ligands had similar bond distances and valence and torsional angles. However, there were some significant differences found, with respect to the coordinated ligand being: (a) the N_{amide}-C_{amide} bond is significantly longer upon coordination; (b) the valence angle of C_{amide}-$C_{methylene}$-C_{amide} is smaller; (c) the $C_{pyridine}$-$C_{methylene}$ bond has a slightly larger torsion; (d) the torsion around the N_{amide}-$C_{methylene}$ bond is significantly different; and (e) the torsion around the C_{amide}-$C_{methylene}$ bond is also significantly different.[4]

The Cu(II) and Ni(II) metal complexes were found to have similar structures. In the case of Cu($papH_2$), the CuN_4 chromophore has a slightly larger tetrahedral twist than the Ni(II) compound. Potentiometric titrations to determine the brutto stability constants of the complexes found that Cu($papH_2$) had a larger stability constant than that of Ni($papH_2$), which "*is in agreement with the larger flexibility towards tetrahedral distortion (d^9 vs low spin d^8)*." They also reported on force-field calculations of Co($papH_2$), Ni($papH_2$), Cu($papH_2$), and Zn($papH_2$), where they were able to obtain a good overall agreement between the varied experimental data sets and the corresponding computed structures.[4]

Kurti *et al.* also reported on the synthesis of **papH$_2$**, which they coordinated to rhenium and technetium for use in nuclear medicine. Structural studies using X-ray analyses, showed Tc and Re complexes have similar geometric structures, as well as similar metal core structures in solution for diamido dipyridino systems. Both metal complexes have a distorted octahedral coordination, with the four nitrogen atoms of the ligand in the equatorial plane and two oxygen atoms occupying the axial positions.[5]

The existing coordination chemistry of **papH$_2$** with these various metals provided inspiration towards donor groups other than pyridyl, such as heteroaromatic (furan) and heterocylic donor (furfuryl) groups. Using a similar ligand structure, it may be possible to coordinate these compounds to the previously discussed metals in order to create catalysts for oxidation and CO_2 carboxylation reactions. As such, this chapter will discuss the synthesis and characterization of six bis(amide) compounds (Figure 3.1) for the eventual coordination to metals to produce potential epoxidation-carboxylation catalysts.



papH$_2$: n = 1 **pabH$_2$**: n = 2 **fapH$_2$**: n = 1 **fabH$_2$**: n = 2 **tapH$_2$**: n = 1 **tabH$_2$**: n = 2

Figure 3.1: The synthesized bis(amide) compounds: *N,N′*-bis[(2-pyridylmethyl)]propanediamide (**papH$_2$**); *N,N′*-bis[(2-pyridylmethyl)]butanediamide (**pabH$_2$**); *N,N′*-bis[(furan-2-ylmethyl)]propanediamide (**fabH$_2$**); *N,N′*-bis[(furan-2-ylmethyl)]butanediamide (**fabH$_2$**); *N,N′*-bis[(tetrahydrofuran-2-ylmethyl)]propanediamide (**tapH$_2$**); *N,N′*-bis[(tetrahydrofuran-2-ylmethyl)]butanediamide (**tabH$_2$**).

3.2 Results and Discussion

The synthesis of **papH$_2$** as described by Comba *et al.*[4] was the starting point of this project. However, heating aqueous diethyl malonate and 2-(aminomethyl)pyridine to reflux overnight did not proceed as outlined in the original report, i.e. only starting materials were recovered. The addition of ethanol and ether to the mixture did not produce the anticipated precipitate. Removal of the organic solvent left behind a viscous red oil that showed only starting material through ^{1}H NMR analysis. A similar procedure described by Kurti *et al.* where ethanol was used as the refluxing solvent[5] also resulted in a similar viscous red oil and analysis of the oil showed only the presence of starting materials and no evidence for product formation.

Based on previous work in the Kerton group on the synthesis of amine-phenol ligands under microwave irradiation,[6] the syntheses of the bis(amide) compounds were attempted using a microwave reactor. Initial attempts employing ethanol as the solvent and its subsequent removal via vacuum, were successful. However, a literature search of ester aminolysis using microwave irradiation showed that many researchers had successfully used solvent-free conditions for related reactions.[7–9] This led to the preparation of the bis(amide) compounds via microwave irradiation under solvent-free conditions (Figure 3.2).

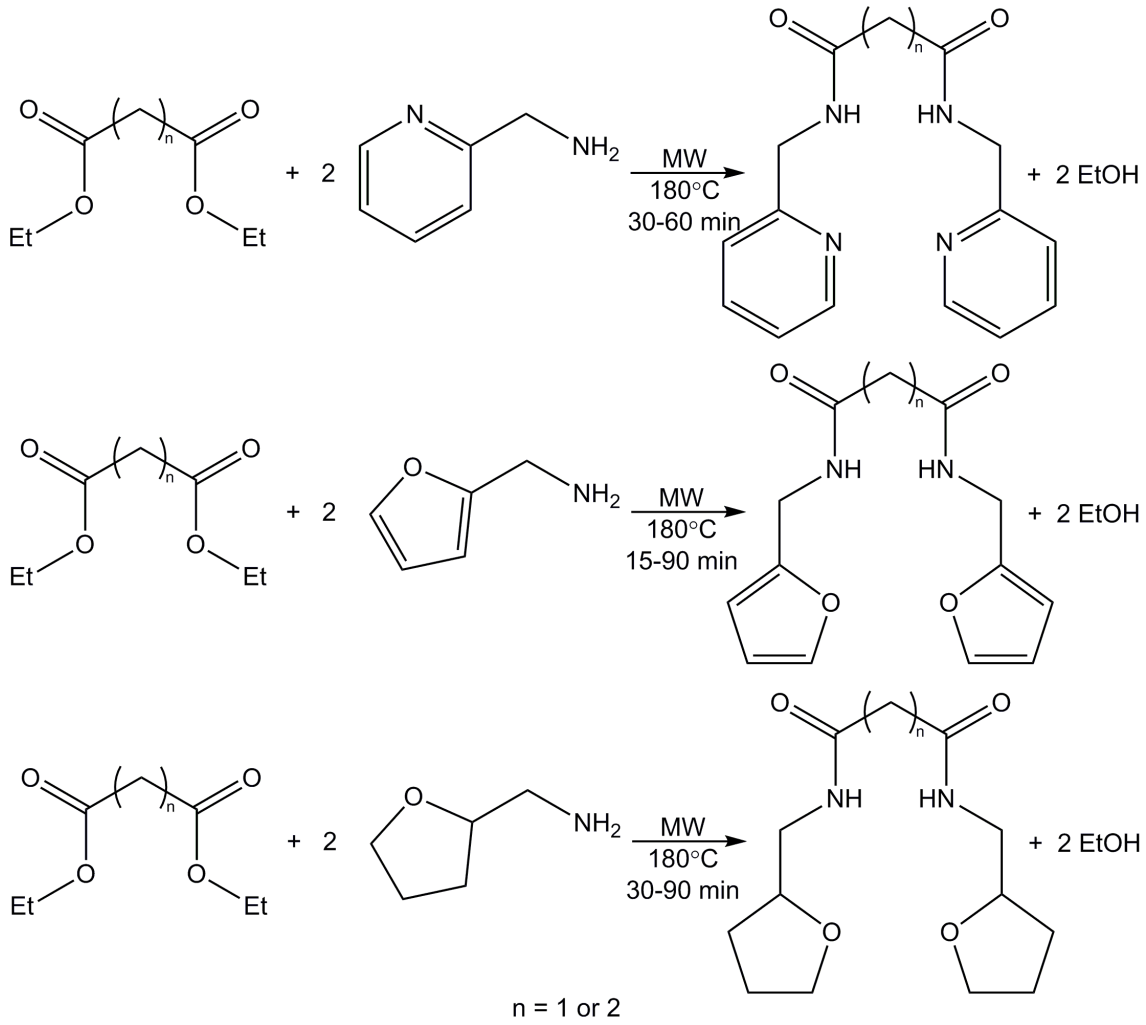


Figure 3.2: General reaction scheme of the synthesis of the various bis(amide) compounds.

In the initial microwave-assisted reactions using ethanol as the solvent, after irradiation, the organic solvent was removed under vacuum. In the case of **fapH$_2$** and **tapH$_2$**, this produced yellow and orange solids, respectively. When washed with ether and filtered, in both cases a white solid was obtained. For the compound **papH$_2$**, it did not solidify, instead it remained a viscous red oil that contained significant amounts of starting material, as was observed for reactions performed using conventional heating methods. However, after it was set aside for two weeks, the oil had solidified to give a

beige solid. When washed with ethyl acetate and filtered, a white solid was obtained. ^{1}H and ^{13}C NMR analysis of these white solids showed the formation of **fapH$_2$**, **tapH$_2$**, and **papH$_2$**.

Soon after these attempts, solvent-free conditions were pursued with varying degrees of success. These reactions were conducted at 180 °C in sealed vials, with varying reactions times (15 to 90 minutes). With the exception of **fabH$_2$**, which fully solidified after irradiation, all the other ligands required time, often overnight, to become fully solid. In the case of **papH$_2$**, it did not solidify over a week, which led to it being placed in the freezer, where crude product was subsequently produced. Interestingly, **tapH$_2$** in the first attempt of its synthesis did solidify overnight after an irradiation of only 15 min at 180 °C. This short reaction time was not always reproducible, so this led to an increase of the reaction time to 30 minutes, which again did not see the mixture solidify, and which led to the use of a freezer to encourage solidification to take place. Once solidified, these crude solids were washed with ether and isolated via filtration, producing varying shades of white and beige crystalline powders (Figure 3.3) with yields up to 85%. They were characterized by ^{1}H and ^{13}C NMR spectroscopy and mass spectrometry (Appendices 4 - 9). The compounds **papH$_2$**, **fapH$_2$**, **tapH$_2$**, and **tabH$_2$** were further characterized by elemental analysis.

Figure 3.3: Purified and isolated **papH$_2$** (A); **pabH$_2$** (B); **fapH$_2$** (C); **fabH$_2$** (D); **tapH$_2$** (E); and **tabH$_2$** (F).

There were some interesting observations made during the synthesis of **fabH$_2$**. The first attempt at the synthesis of this ligand was also the first time diethyl succinate was used in this research. As such, the synthesis was attempted at 180 °C for 15 minutes. However, it was observed that no precipitate had formed, even after irradiating the mixture again at 200 °C for 15 minutes. A miniscule amount of solid (0.5%) was obtained from the mixture after 5 days in the freezer. However, after approximately 2 months, the filtrate was observed to have solidified into a brown crystalline solid, that when washed with ether and filtered, produced a 44% yield of the desired ligand.

In subsequent attempts, the reaction time was increased to 60 minutes with any reaction using diethyl succinate, as it appeared to require more time under microwave irradiation to react. These attempts produced yields up to 2.4%, which also required the mixture to be set aside overnight in order to solidify. In order to improve the yield of **fabH$_2$**, the reaction time was further increased to 90 minutes, whereupon a solid was produced immediately after irradiation and cooling to room temperature, and an 8% yield

was obtained. In a separate reaction, after the solid had been washed and filtered, the filtrate was put under vacuum to remove the ether. After that, a ^{1}H NMR analysis was done where it was observed that the filtrate contained both starting material and product.

It was also observed that **fabH$_2$**, in contrast to the other ligands prepared, was not soluble in either acetone or $CDCl_3$, leading to CD_3OD being used as the solvent for NMR analysis. This accounts for the amine proton peak missing from the spectrum, as the amine protons exchanged with the deuterium in the NMR solvent. (Appendix 7).

The ^{1}H NMR spectra of four of the six compounds prepared could be readily assigned however, **tapH$_2$** and **tabH$_2$** required 2D NMR techniques. COSY and HSQC NMR were used to fully assign each environment within these compounds. This is due to complexities arising from coupling between protons around the saturated heterocyclic rings.

Single crystals of **tabH$_2$** suitable for X-ray diffraction were grown by slow evaporation of an ether solution at room temperature. The ORTEP plot (Figure 3.4) shows the ligand oriented such that the amides are *trans* to one another. H-bonding occurs between neighbouring molecules within the crystal lattice, between the amide proton of one ligand and the amide oxygen of another. The molecule is centrosymmetric with the inversion centre located between C1 and C1*.

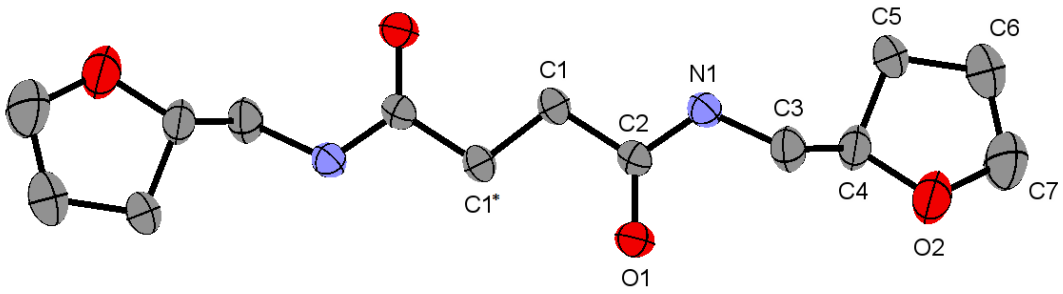


Figure 3.4: Molecular structure of **tabH$_2$**. The displacement ellipsoids are drawn at the 50% probability level. H atoms are excluded for clarity.

Table 3.1: Summary of crystal data for ligand **tabH$_2$**.

Compounds	**tabH$_2$**
Formula	$C_{14}H_{22}N_2O_4$
Formula Weight	284.36
Crystal System	Monoclinic
Space Group	I 2/a
a	9.5510(10) Å
b	4.6804(4) Å
c	32.256(3) Å
α	90°
β	93.899(10)°
γ	90°
V	1438.59 Å^3
T	293 K
Z	4
D_c	1.313 g/cm^3
F(000)	616
μ(MoKα)	0.96 cm^{-1}
Total Reflections	10029
Unique Reflections	1814
R_{int}	0.061
Reflections $I > 2\sigma(I)$	1474
No. of parameters	140
R, wR_2 [$I > 2\sigma(I)$]	0.0933, 0.0992
Goodness of Fit	0.7925

Table 3.2: Selected bond distances (Å) and angles (°) for **tabH$_2$**.

N(1)-C(2)	1.328(5)	O(1)-C(2)-N(1)	122.1(3)
N(1)-C(3)	1.457(4)	O(1)-C(2)-C(1)	122.6(3)
O(1)-C(2)	1.231(4)	C(2)-N(1)-C(3)	122.6(3)
O(2)-C(4)	1.453(5)	C(4)-O(2)-C(7)	106.4(4)
O(2)-C(7)	1.432(7)		

3.3 Conclusions

In conclusion, six bis(amide) compounds have been successfully synthesized through microwave irradiation under solvent-free conditions whose workups involved straightforward washing with ether and filtration. Up to 85% yields have been obtained, which when paired with the appropriate metal, may provide suitable catalysts for oxidation and carboxylation reactions. Compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, melting points, and in some cases, elemental microanalytical data were obtained.

The next step would be the coordination of these compounds to various metals. There are a number of metals to choose from. Adolph *et al.* who used amide ligands for the coupling reaction of epoxides to carbon dioxide, used cobalt, iron, and chromium.[3] Comerford *et al.* reviewed the synthesis of five-membered cyclic carbonates using catalysts of the abundant metals: potassium, aluminum, sodium, calcium, titanium, and iron.[1] The metals chosen for coordination, would then be tested in epoxidation and carboxylation reaction of alkenes to cyclic carbonates. Structural studies would also be accomplished for the metal catalysts, along with the metal-free ligands.

3.4 Experimental

3.4.1 Materials and Instruments

Diethyl malonate, diethyl succinate, 2-(aminomethyl)pyridine, furfurylamine, and tetrahydrofurfurylamine were obtained from Alfa Aesar. Ether and ethyl acetate were obtained from ACP Chemicals Inc. Anhydrous ethanol was obtained from Commercial Alcohols. Deuterated solvents were purchased from Cambridge Isotope Laboratory Inc. Microwave vials, caps, and stir bars were purchased from Biotage.

All experiments were performed using a microwave (Biotage Initiator 2.5). Elemental analyses were performed by Ocean Sciences Centre, Memorial University, or Saint Mary's University. NMR spectra were recorded on a Bruker AVANCE III 300 MHz spectrometer at 298 K and were referenced internally using the residual ^{1}H and ^{13}C resonances of the solvent. Melting points were obtained using an OptiMelt Automatic Melting Point System. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) experiments were performed using an Applied Biosystems 4800 MALDI TOF/TOF Analyzer, using DHBA as the matrix.

3.4.2 Ligand Syntheses

$papH_2$ (*N,N′*-bis[(2-pyridylmethyl)]propanediamide): Diethyl malonate (1.00 g, 6.25 mmol) and 2-(aminomethyl)pyridine (1.35 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 30 min at 180 °C, resulting in a dark red solution. The mixture

was set in the freezer for two days, upon which a beige solid formed. Ether was used to wash the solid, and upon filtration afforded a beige solid.

Yield: 53%.

MP: 93.7-94.5 °C.

Anal. calcd. for $C_{15}H_{16}N_4O_2$: C 63.37, H 5.67, N 19.71. **Found:** C 63.59, H 5.64, N 19.71.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.48 (m, 2H, CHNC), 8.17 (s, 2H, NH), 7.59 (td, 2H, *J* = 7.7, 1.8 Hz, CHCHCH), 7.21 (m, 2H, CHCHCH), 7.13 (m, 2H, CHCHCH), 4.54 (d, 4H, *J* = 5.3 Hz, $NHCH_2$), 3.35 (s, 2H, CH_2).

^{13}C NMR ($CDCl_3$, 300 MHz): δ 164.5 (C=O), 156.5 ($NC(CH_2)CH$), 149.2 (CHNC), 136.8 ($C(CH_2)CHCH$), 122.4 (CHCHCH), 121.9 (CHCHCH), 44.8 ($NHCH_2$), 43.1 ($CH_2C{=}O$).

pabH$_2$ (*N,N′*-bis[(2-pyridylmethyl)]butanediamide): Diethyl succinate (1.09 g, 6.25 mmol) and 2-(aminomethyl)pyridine (1.35 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 60 min at 180 °C. Setting aside for 16 hours allowed the formation of an dark yellow solid. Ether was used to wash the solid, and upon filtration afforded a fluffy, white solid.

Yield: 61%.

MP: 137.1 - 137.6 °C.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.46 (ddd, 2H, *J* = 4.9, 1.8, 1.0 Hz, NC<u>H</u>CH), 7.57 (td, 2H, *J* = 7.7, 1.8 Hz, C<u>H</u>CHC), 7.42 (t, 2H, *J* = 5.4 Hz, N<u>H</u>), 7.20 (m, 2H, CHC<u>H</u>C), 7.12 (ddd, 2H, *J* = 7.5, 4.9, 1.1 Hz, NCHC<u>H</u>), 4.49 (d, 4H, *J* = 5.3 Hz, NHC<u>H$_2$</u>C), 2.62 (s, 4H, C<u>H$_2$</u>C=O).

^{13}C NMR ($CDCl_3$, 300 MHz): δ 172.3 (<u>C</u>=O), 156.9 (N<u>C</u>(CH$_2$)CH)), 149.0 (<u>C</u>HNC), 136.7 (CCH<u>C</u>H), 122.2 (<u>C</u>HCHN), 121.9 (C<u>C</u>HCH), 44.7 (NH<u>C</u>H$_2$), 31.6 (<u>C</u>H$_2$C=O).

fapH$_2$ (*N,N′*-bis[(furan-2-ylmethyl)]propanediamide): Diethyl malonate (1.00 g, 6.25 mmol) and furfurylamine (1.21 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 15 min at 180 °C, afterwards producing a brown solid. Ether was used to wash the solid, and upon filtration afforded a white powder.

Yield: 85%.

MP: 122.0 - 123.8 °C.

Anal. calcd for $C_{13}H_{14}N_2O_4$: C 59.54, H 5.38, N 10.68. **Found:** C 59.51, H 5.42, N 10.69.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.65 (s, 2H, N<u>H</u>), 7.31 (dd, 2H, *J* = 1.9, 0.8 Hz, COC<u>H</u>), 6.28 (dd, 2H, *J* = 3.2, 1.9 Hz, C<u>H</u>CHC), 6.18 (dd, 2H, *J* = 3.2, 0.7 Hz, CHC<u>H</u>C), 4.38 (d, 4H, *J* = 5.6 Hz, NHC<u>H$_2$</u>C), 3.20 (s, 2H, CC<u>H$_2$</u>C).

^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.3 (C=O), 150.9 (OC(CH_2)CH), 142.4 (CHOC(CH_2)CH), 110.5 (CHCHC), 107.6 (CHCHC), 42.7 (CH_2C=O), 36.6 (NHCH_2).

fabH$_2$ (*N,N′*-bis[(furan-2-ylmethyl)]butanediamide): Diethyl succinate (1.09 g, 6.25 mmol) and furfurylamine (1.21 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 90 min at 180 °C, upon which produced a yellow solid. Ether was used to wash the solid, and upon filtration afforded a sparkly, white powder.

Yield: 44%.

MP: 186.8 - 188.7 °C.

^{1}H NMR (CD_3OD, 300 MHz): δ 7.40 (m, 2H, CHOC), 6.33 (m, 2H, CHCHCH), 6.23 (m, 2H, CHCHCH), 4.33 (s, 4H, CH_2C=O), 2.50 (s, 4H, NHCH_2).

^{13}C NMR (CD_3OD, 300 MHz): δ 174.4 (C=O), 153.1 (OC(CH_2)CH), 143.3 (CHOC), 111.3 (CHCHCH), 108.0 (CHCHCH), 37.2 (NHCH_2), 32.0 (CH_2C=O).

tapH$_2$ (*N,N′*-bis[(tetrahydrofuran-2-ylmethyl)]propanediamide): Diethyl malonate (1.00 g, 6.25 mmol) and tetrahydrofurfurylamine (1.21 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 30 min at 180 °C resulting in a clear, orange solution. The

mixture was set in the freezer, and after a day a solid was formed. Ether was used to wash the solid, and upon filtration afforded a white powder.

Yield: 66%.

MP: 71.6 - 72.9 °C.

Anal. calcd for $C_{13}H_{22}N_2O_4$: C 57.76, H 8.20, N 10.36. **Found:** C 57.86, H 8.10, N 10.41.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.26 (s, 2H, NH), 3.94 (qd, 2H, *J* = 7.0, 3.8 Hz, CH), 3.81 (m, 2H, OCH(H)), 3.70 (m, 2H, OCH(H)), 3.48 (ddd, 2H, *J* = 13.7, 6.1, 3.7 Hz, NHCH(H)), 3.17 (m, 4H, CCH_2C, NHCH(H)), 1.90 (m, 6H, $CH_2CH(H)CH$), 1.51 (m, 2H, $CH_2CH(H)CH$).

^{13}C NMR ($CDCl_3$, 300 MHz): δ 167.5 (C=O), 77.5 (CH), 68.2 (CH_2OCH), 43.4 (CH_2), 43.0 (CH_2), 28.8 (CH_2CH_2CH), 25.9 (CH_2CH_2CH).

tabH$_2$ (*N,N′*-bis[(tetrahydrofuran-2-ylmethyl)]butanediamide): Diethyl succinate (1.09 g, 6.25 mmol) and tetrahydrofurfurylamine (1.21 g, 12.5 mmol) were added to a 5 mL microwave vial equipped with a stir bar. The resulting mixture was then subjected to microwave irradiation for 90 min at 180 °C resulting in a clear, yellow solution. After three hours, a solid had formed. Ether was used to wash the solid, and upon filtration afforded a fluffy, white solid.

Yield: 21%.

MP: 136.4-139.5 °C.

Anal. calcd for $C_{14}H_{24}N_2O_4$: C 59.14, H 8.51, N 9.85. **Found:** C 59.44, H 8.49, N 9.86.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.36 (s, 2H, NH), 3.91 (m, 2H, OCH(CH_2)CH_2), 3.82 (m, 2H, CH(H)OCH), 3.70 (m, 2H, CH(H)OCH), 3.49 (m, 2H, NHCH(H)), 3.12 (m, 2H, NHCH(H)), 2.50 (m, 4H, CH_2C=O), 1.89 (m, 6H, OCHCH(H)CH_2), 1.49 (m, 2H, OCHCH(H)CH_2).

^{13}C NMR ($CDCl_3$, 300 MHz): δ 172.3 (C=O), 77.8 (OCH(CH_2)CH_2), 68.1 (CH_2OCH), 43.3 (NHCH_2), 31.8 (CH_2C=O), 28.7 (OCH(CH_2)CH_2), 25.9 (CH_2CH_2O).

3.5 References

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(7) Zradni, F.-Z.; Hamelin, J.; Derdour, A. *Synth. Commun.* **2002**, *32*, 3525–3531.

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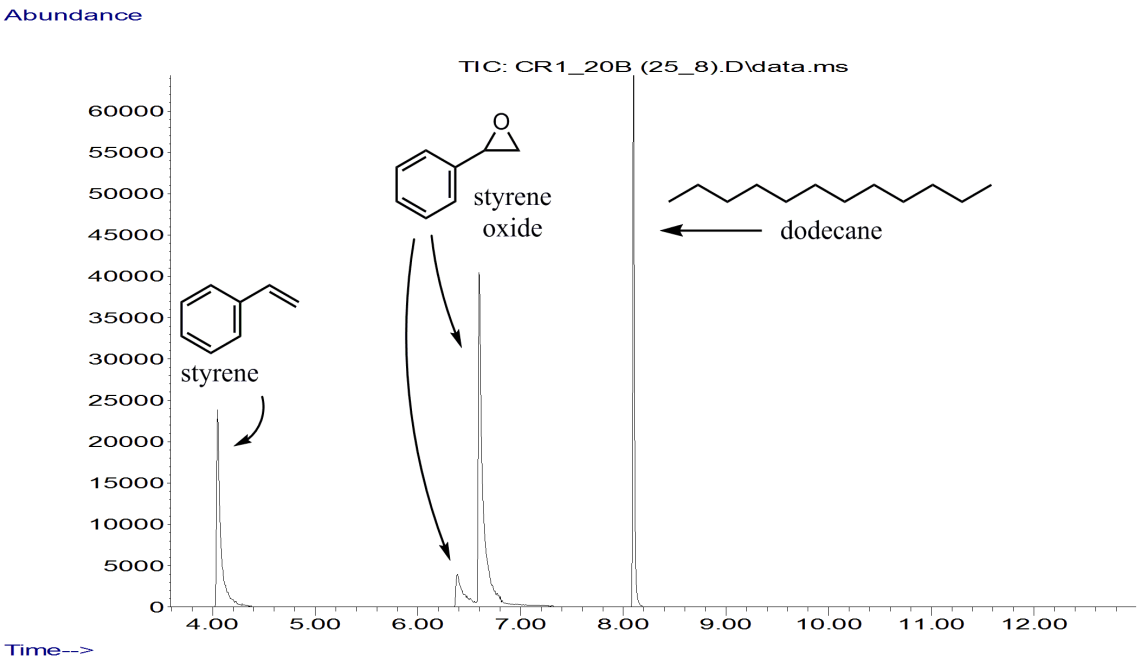
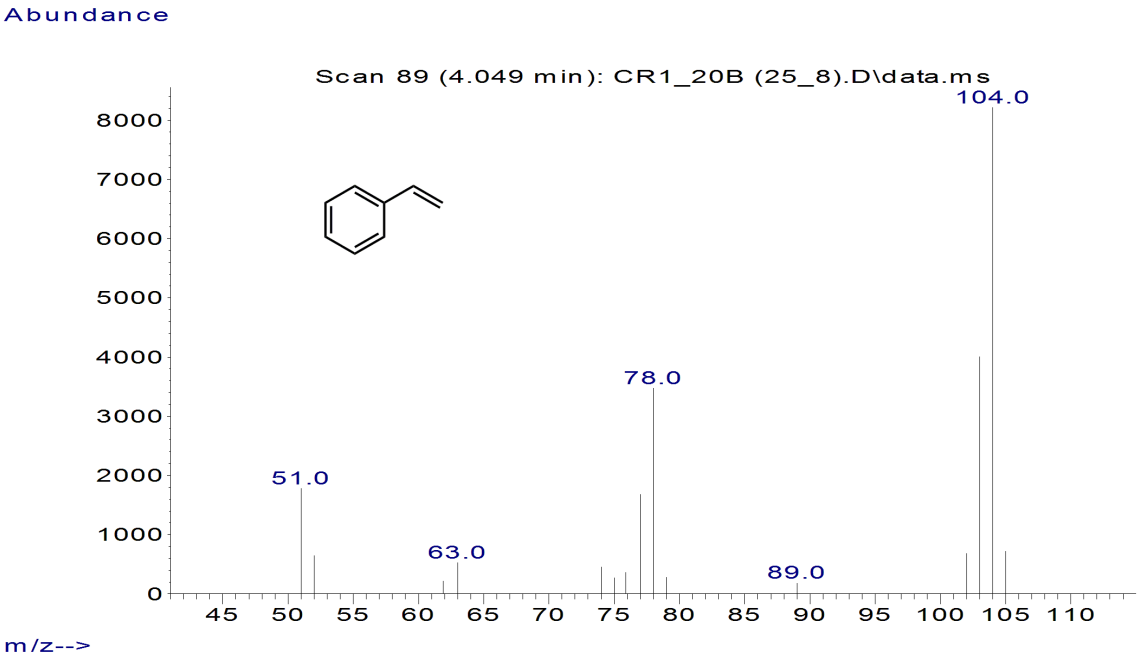
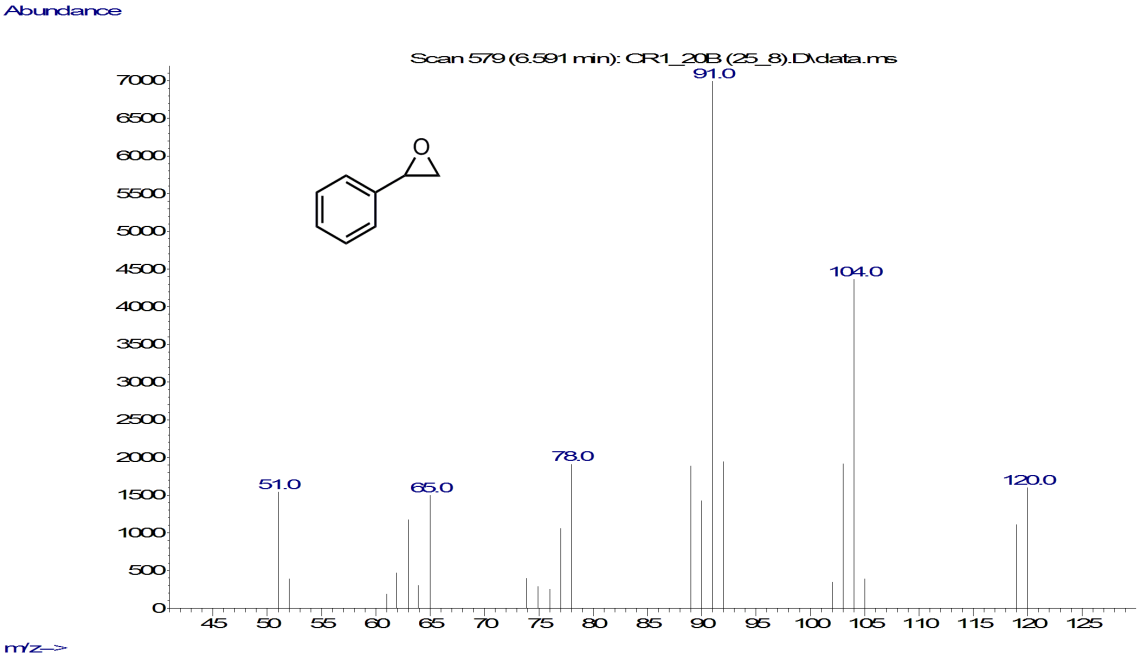
(9) Ramesh, P.; Fadnavis, N. W. *Chem. Lett.* **2015**, *44* (2), 138–140.

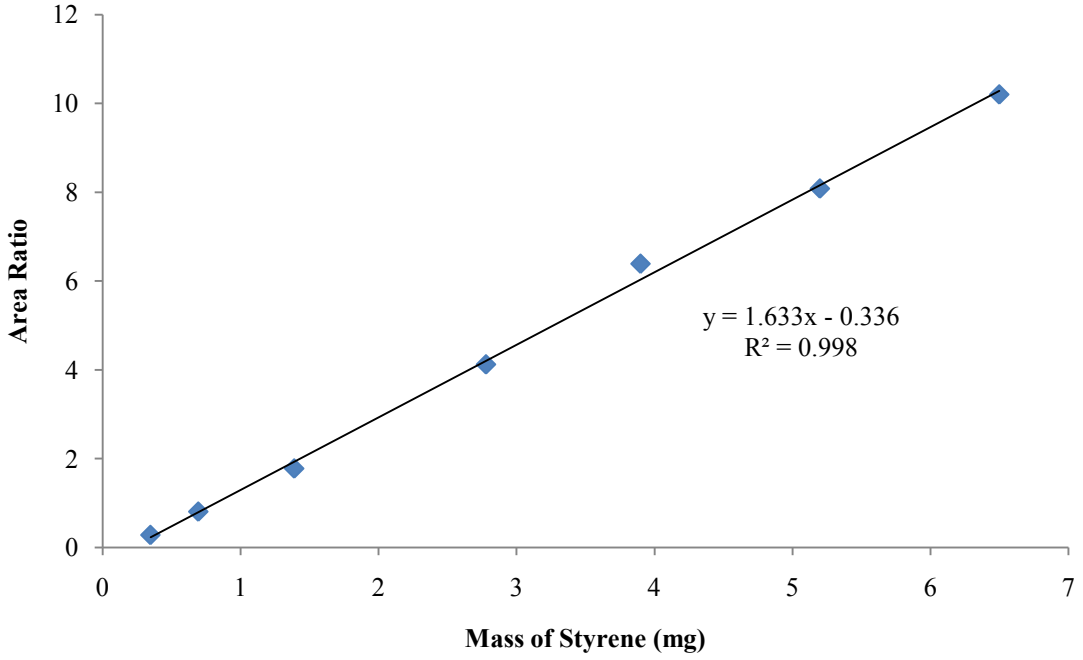
APPENDIX 1: Example GC-MS - chromatogram and mass spectra of styrene and styrene oxide

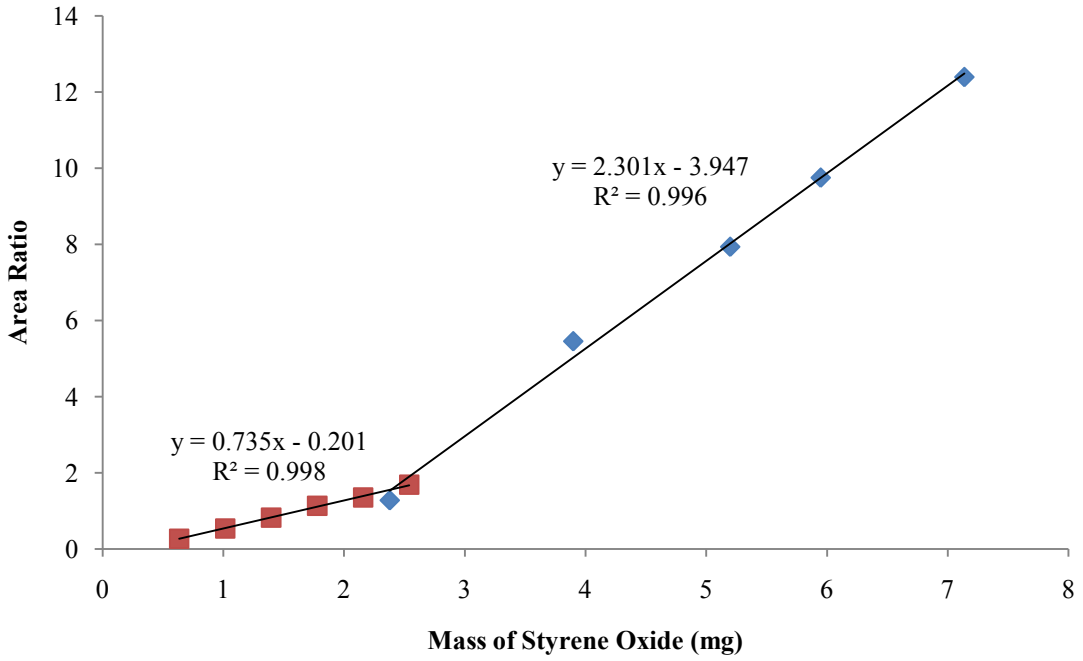




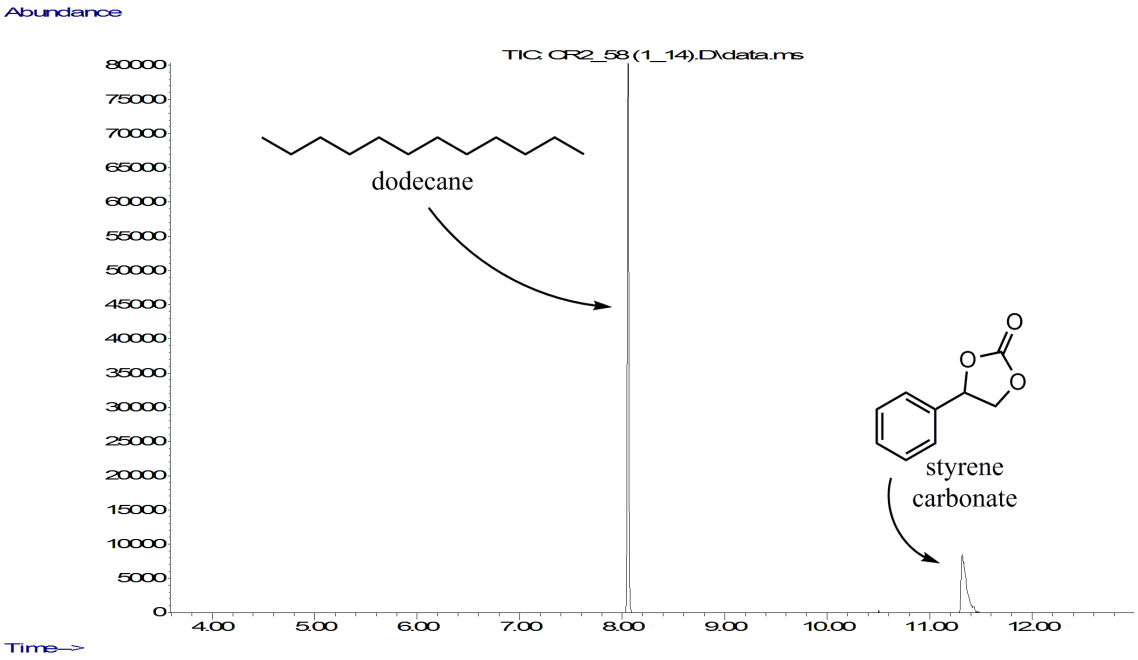

Abundance
Scan 579 (6.591 min): CR1_20B (25_8).D\data.ms
91.0
104.0
78.0
51.0
65.0
120.0
m/z-->

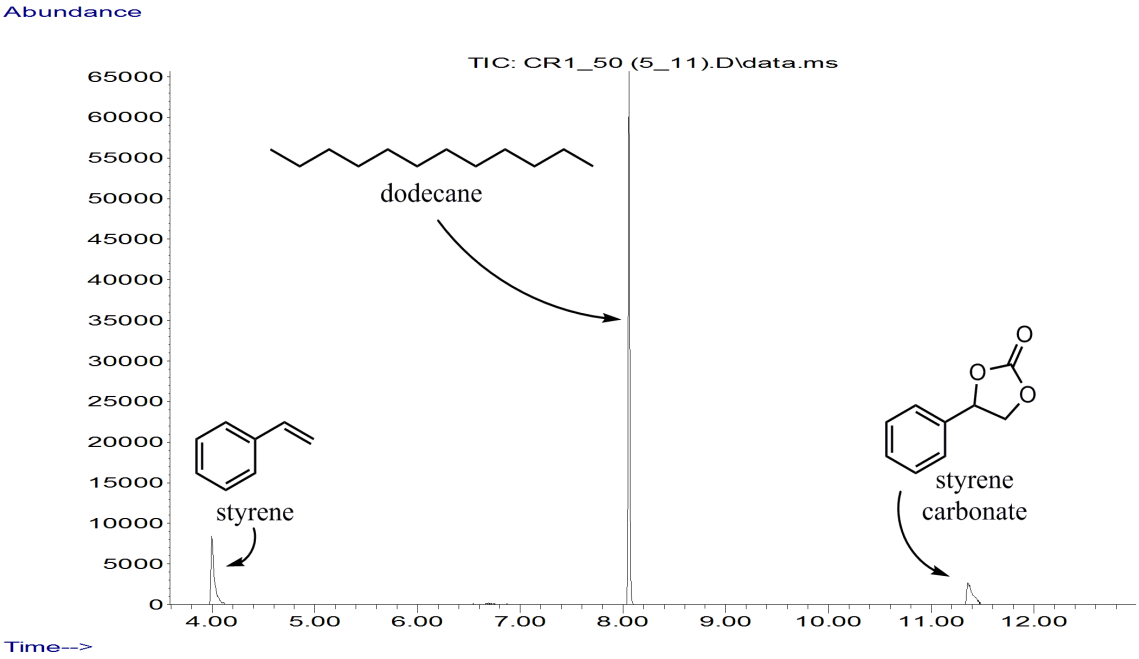
APPENDIX 2: Calibration curve for the determination of the conversion of styrene (top) and the yield of styrene oxide (bottom) using dodecane as an internal standard.





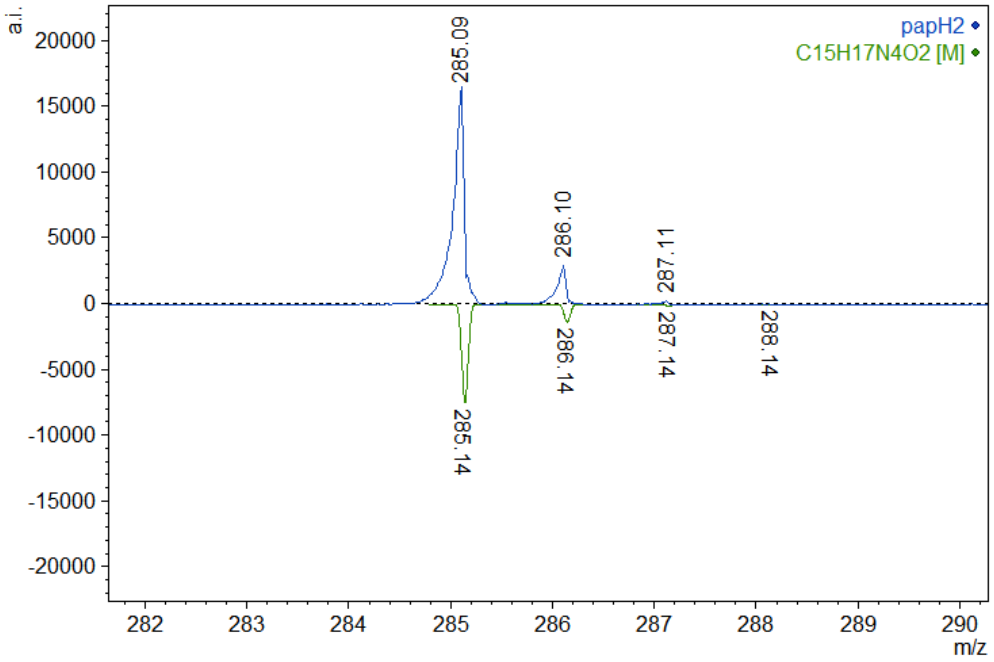
APPENDIX 3: GC-MS chromatograms of the cycloaddition of CO_2 to styrene oxide at atmospheric pressure: separate epoxidation reaction that was refluxed (top) and one-pot reaction mixture (bottom)



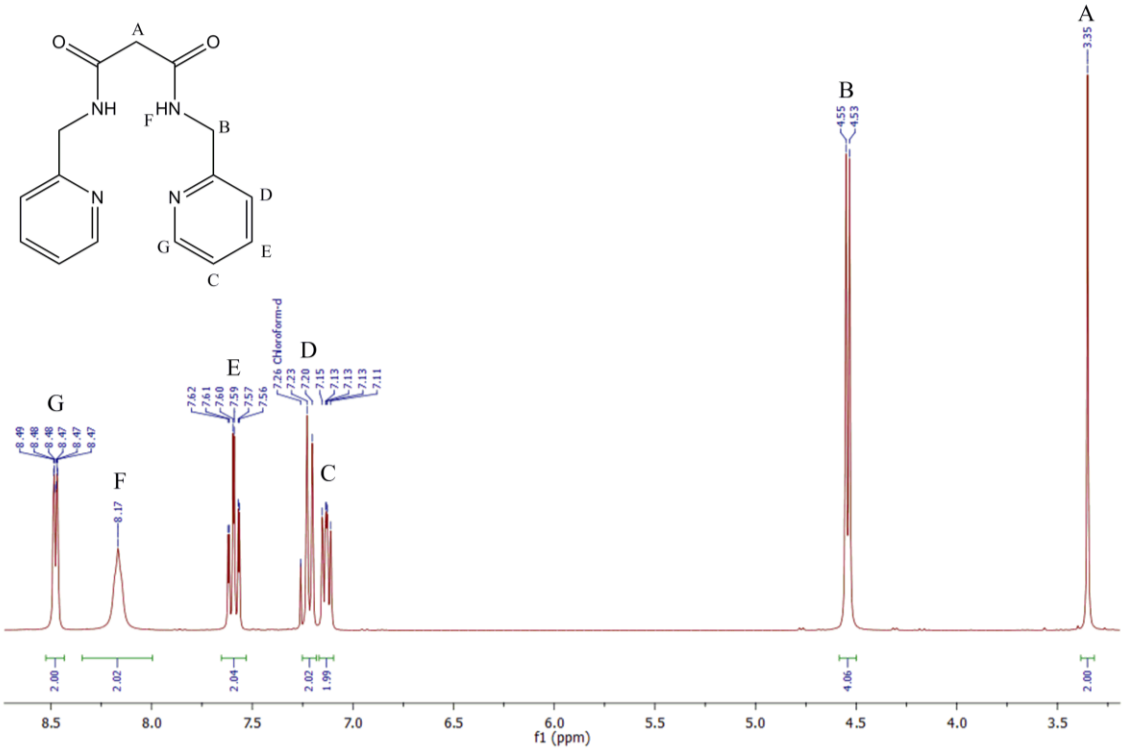


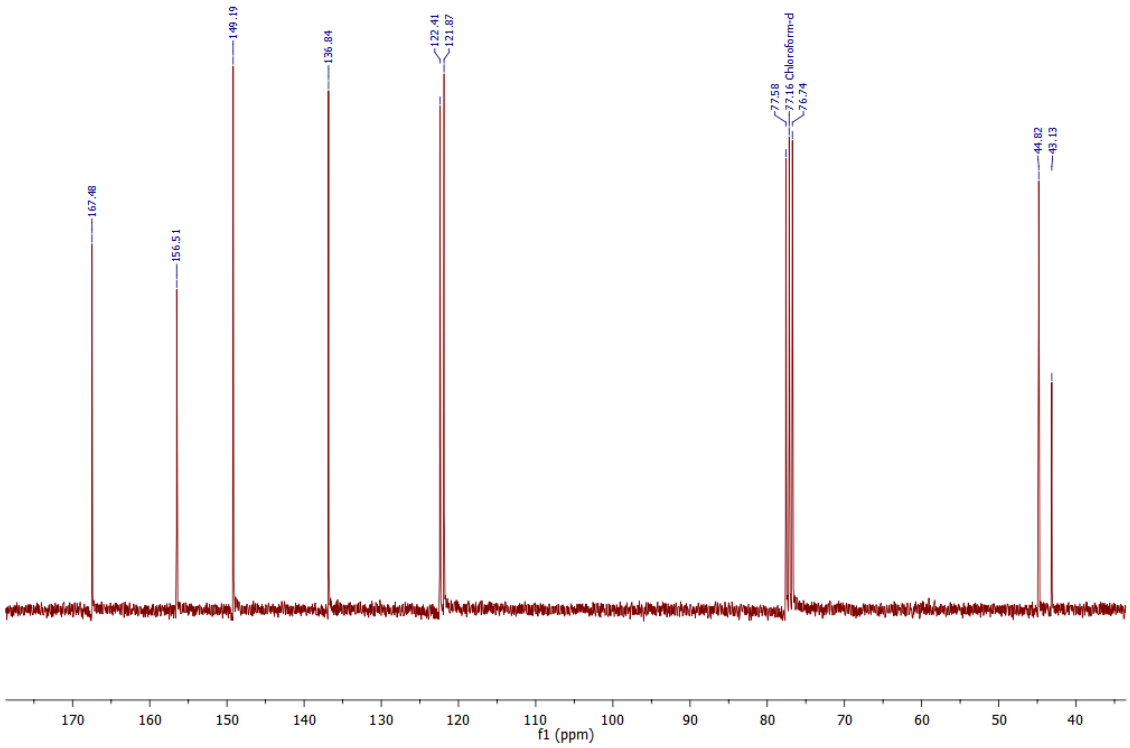
APPENDIX 4: $papH_2$

MALDI-TOF mass spectrum of **$papH_2$** (top) and calculated mass (bottom)



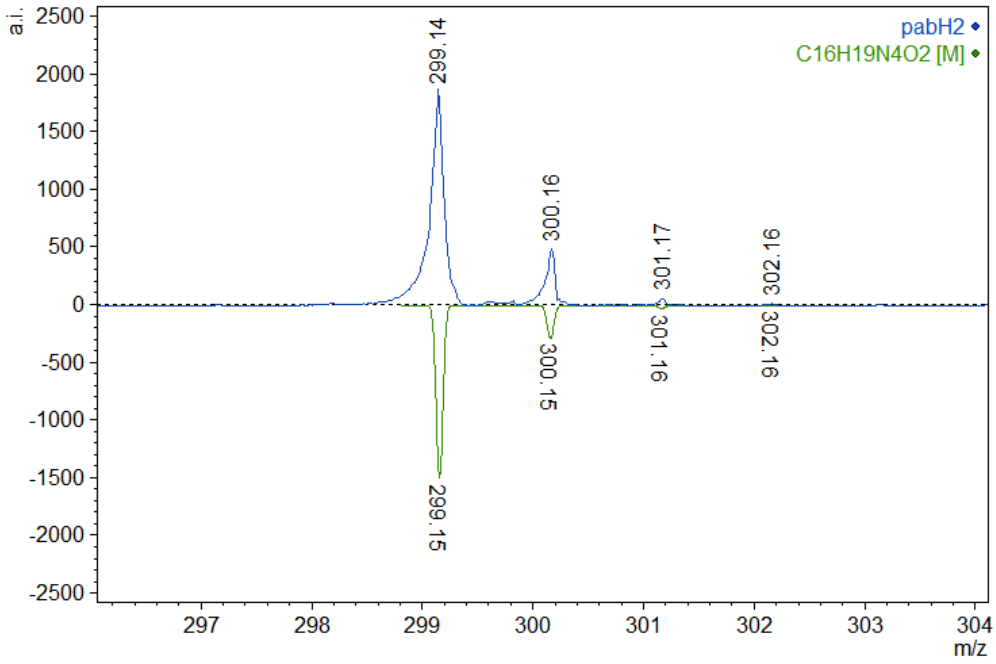
^{1}H and ^{13}C NMR spectra of **$papH_2$** in $CDCl_3$.



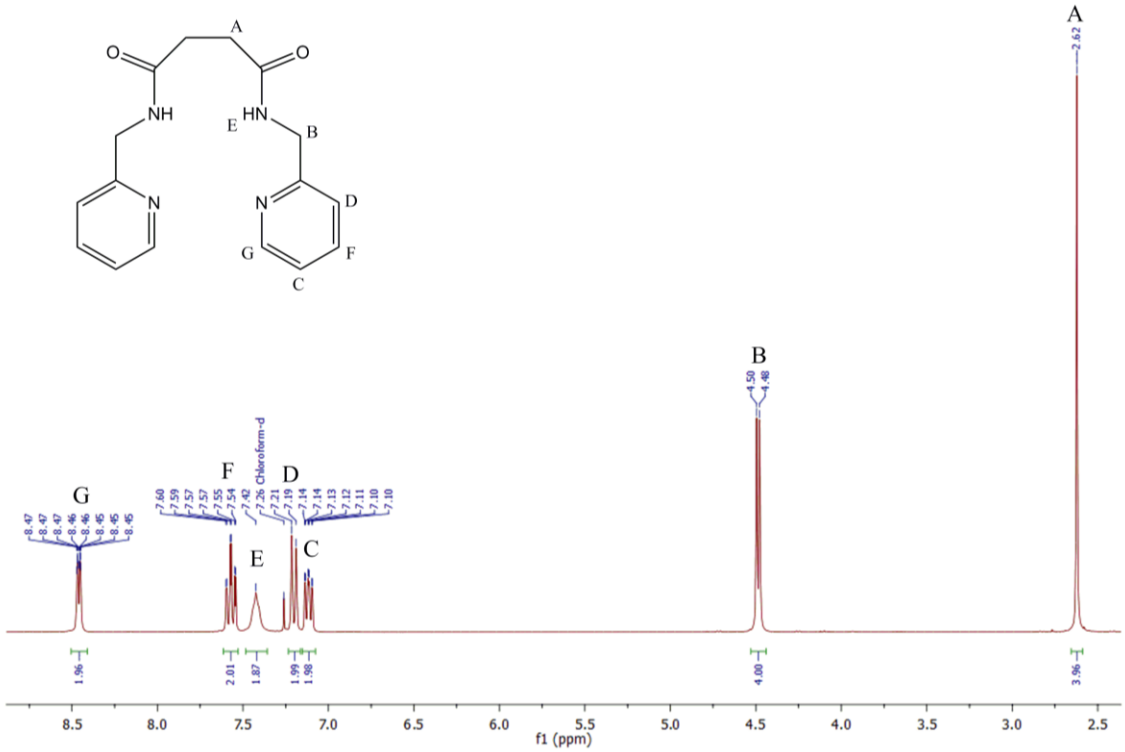

167.48
156.51
149.19
136.84
122.41
121.87
77.58
77.16 Chloroform-d
76.74
44.82
43.13
170
160
150
140
130
120
110
100
90
80
70
60
50
40
f1 (ppm)

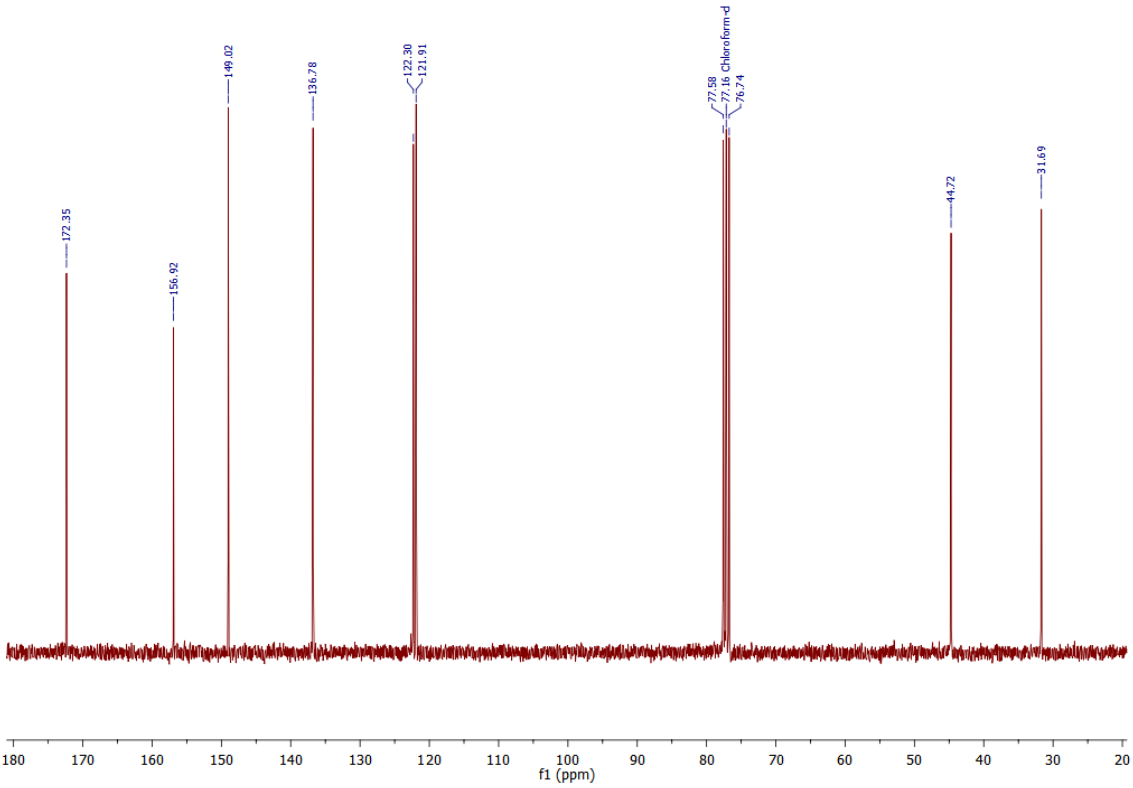
APPENDIX 5: $pabH_2$

MALDI-TOF mass spectrum of **$pabH_2$** (top) and calculated mass (bottom).



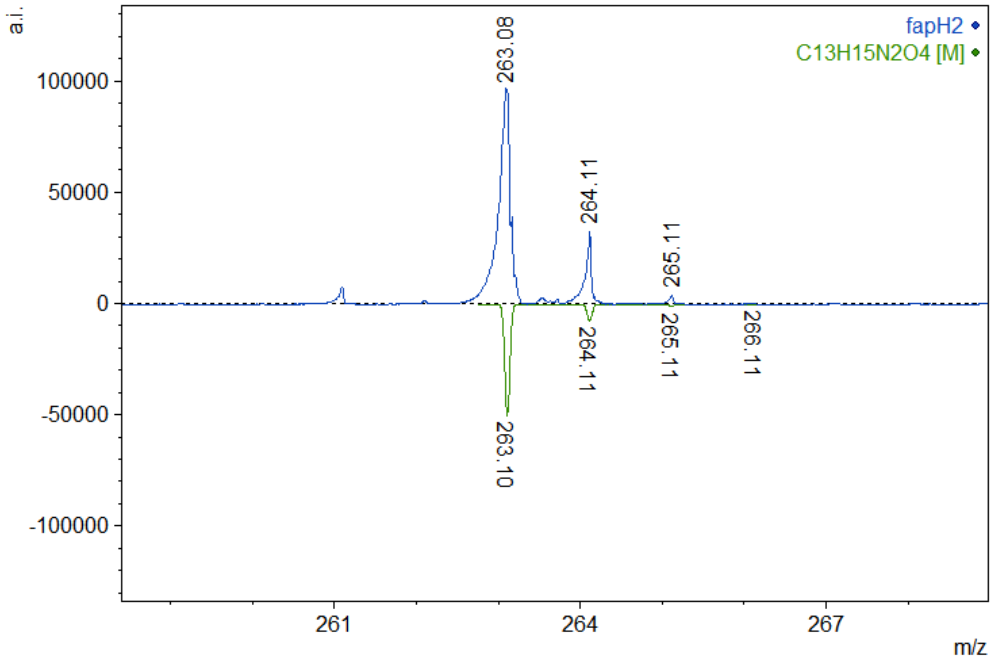
^{1}H and ^{13}C NMR spectra of **$papH_2$** in $CDCl_3$.



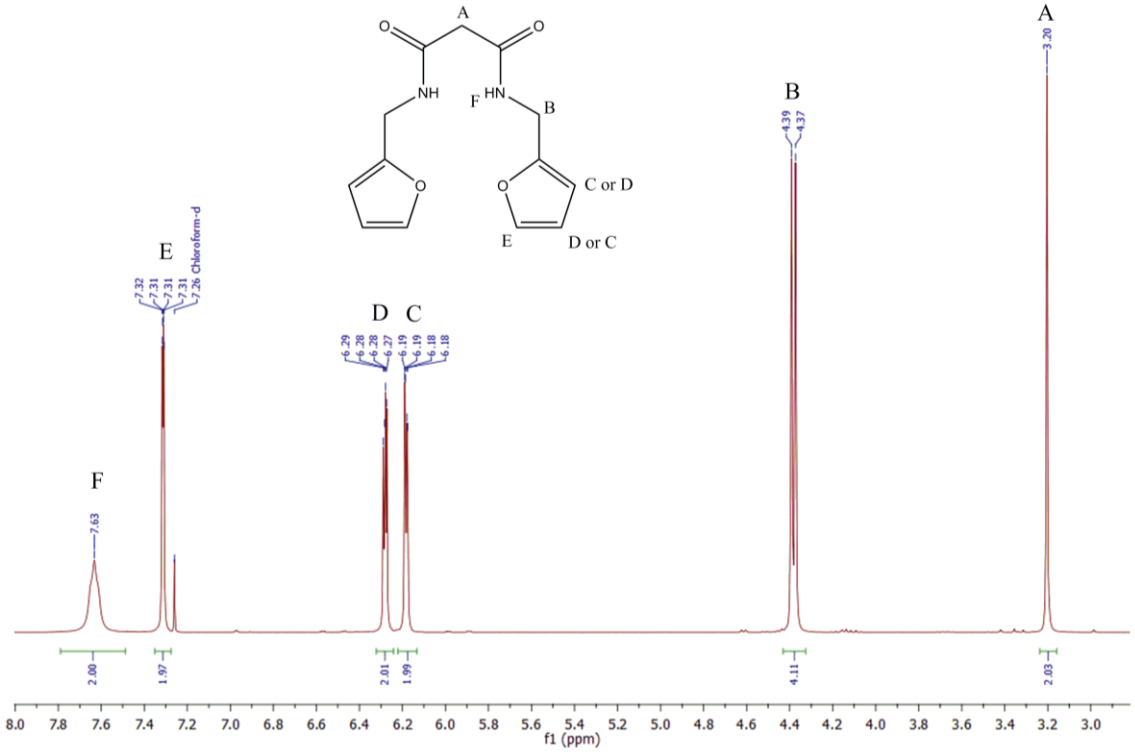

172.35
156.92
149.02
136.78
122.30
121.91
77.58
77.16 Chloroform-d
76.74
44.72
31.69
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

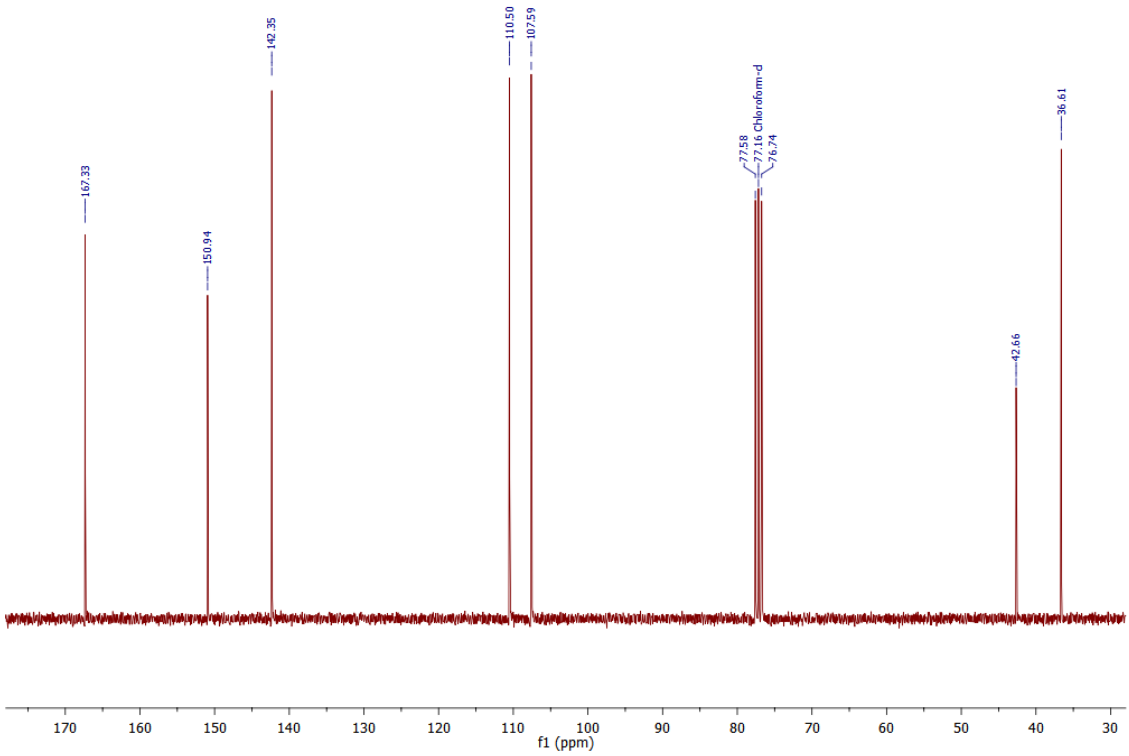
APPENDIX 6: $fapH_2$

MALDI-TOF mass spectrum of **$fapH_2$** (top) and calculated mass (bottom).



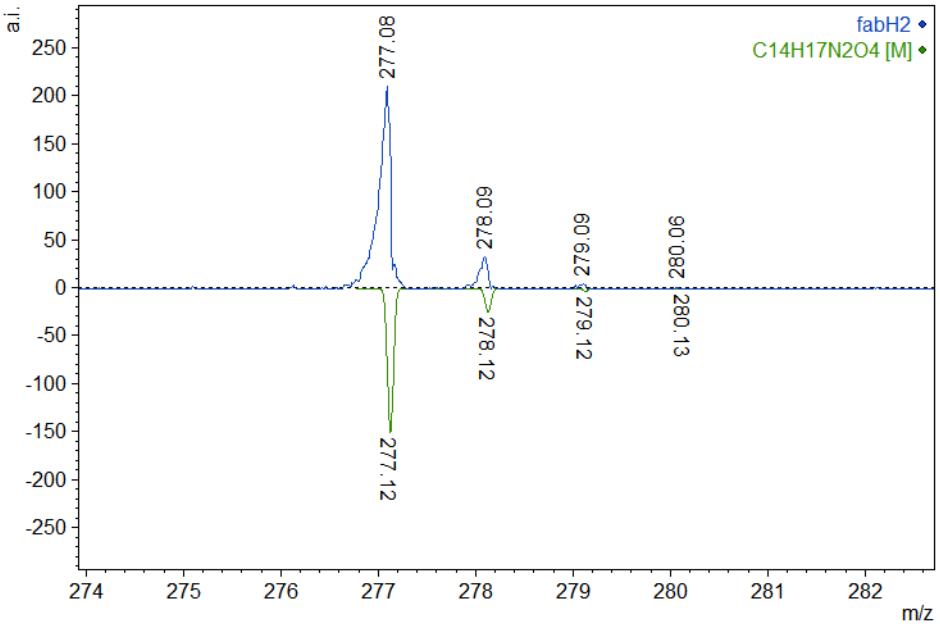
^{1}H and ^{13}C NMR spectra of **$fapH_2$** in $CDCl_3$.



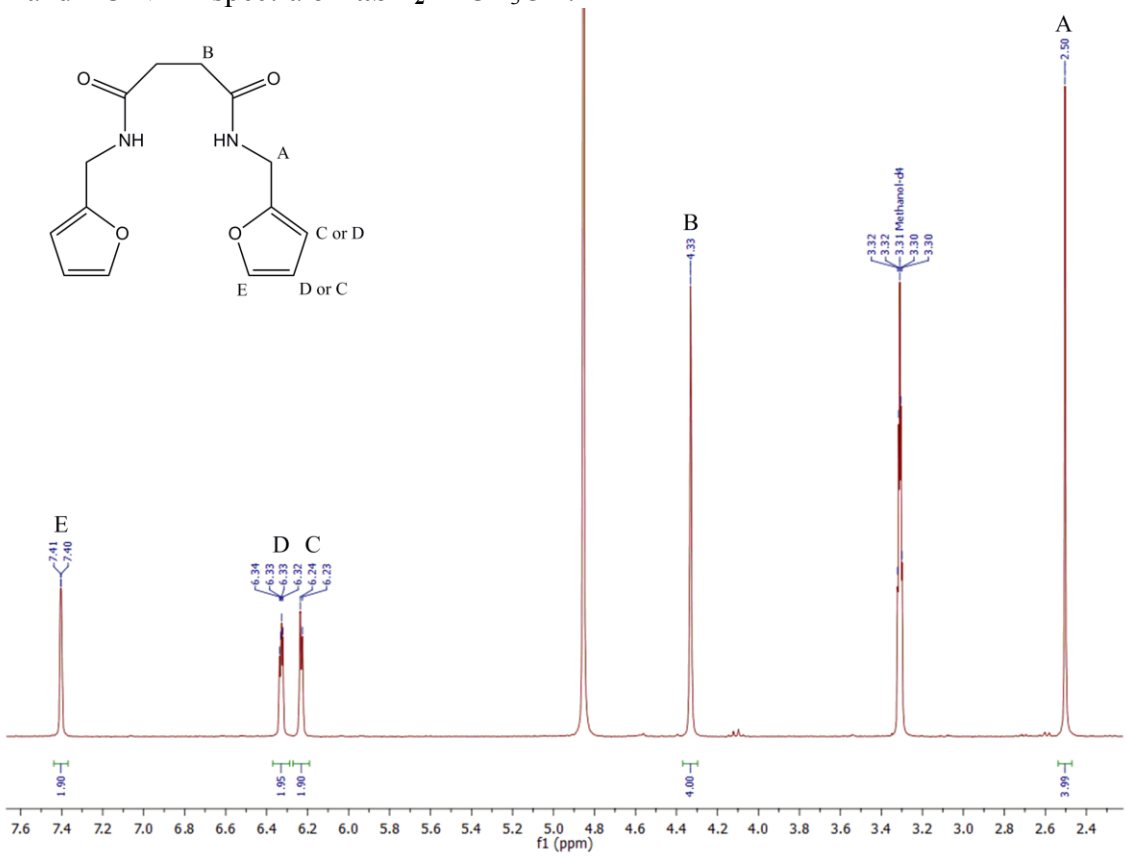

167.33
150.94
142.35
110.50
107.59
77.58
77.16 Chloroform-d
76.74
42.66
36.61
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

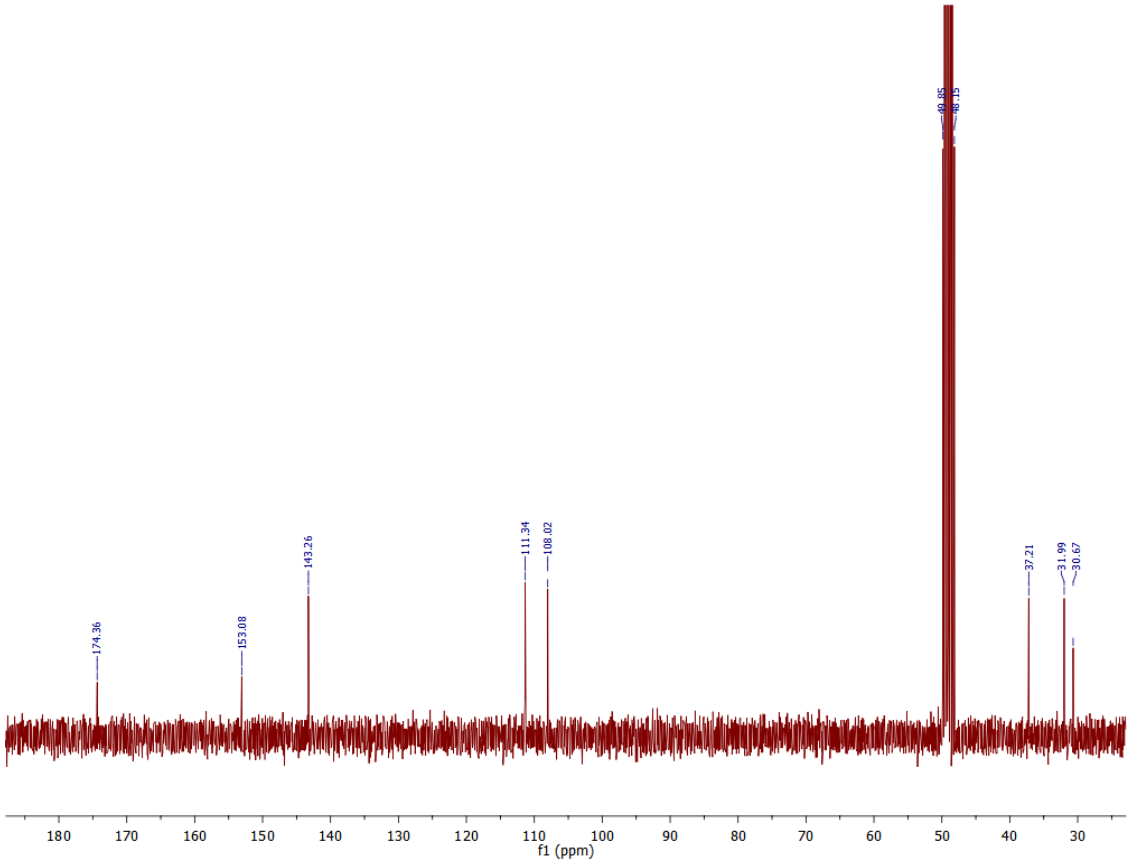
APPENDIX 7: $fabH_2$

MALDI-TOF mass spectrum of **$fabH_2$** (top) and calculated mass (bottom).



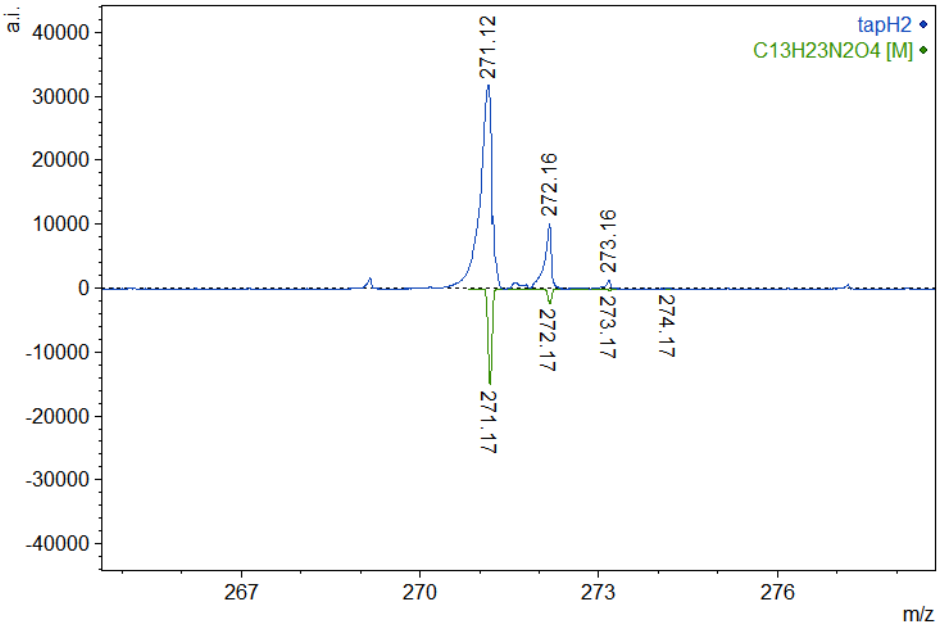
^{1}H and ^{13}C NMR spectra of **$fabH_2$** in CD_3OD.



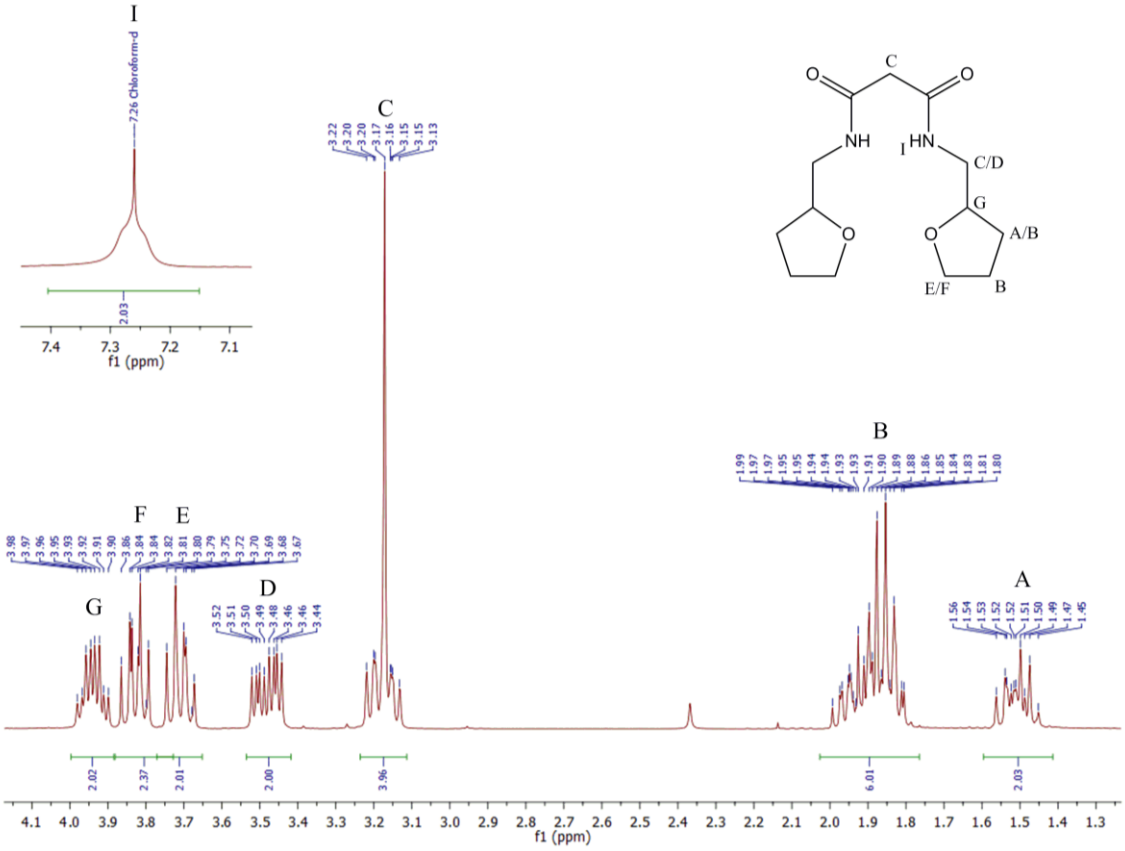

174.36
153.08
143.26
111.34
108.02
49.85
48.15
37.21
31.99
30.67
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

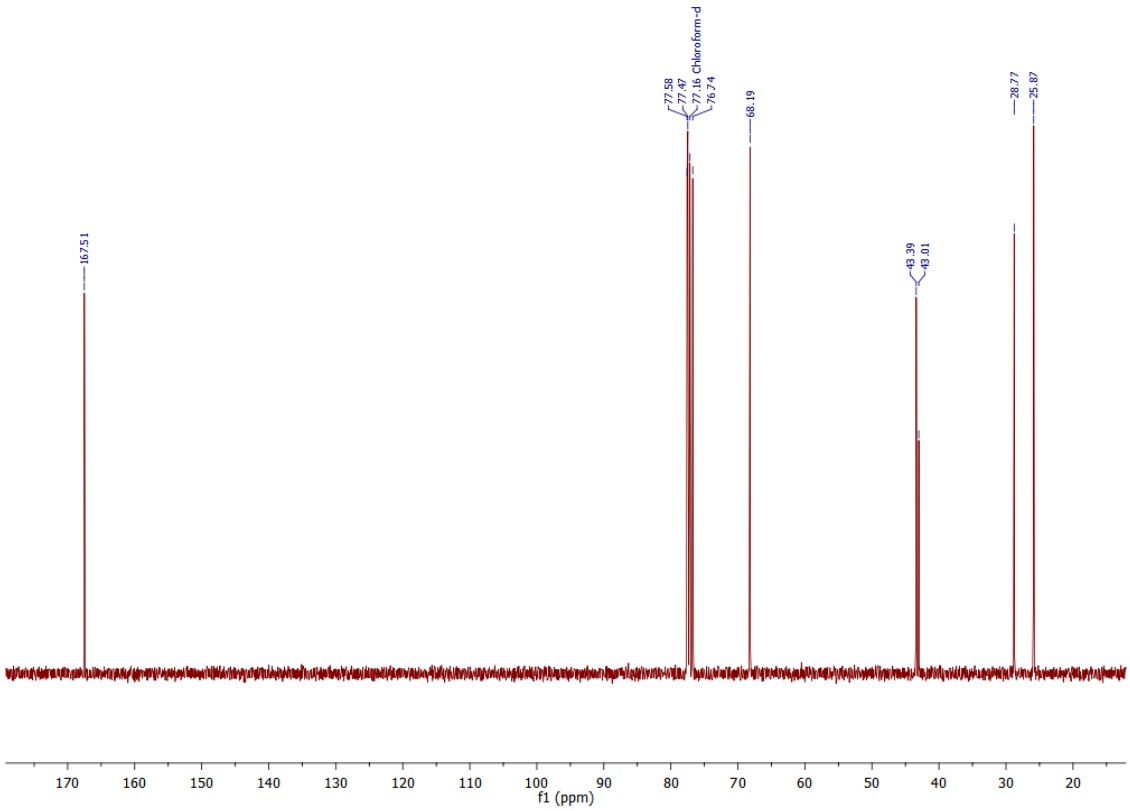
APPENDIX 8: $tapH_2$

MALDI-TOF mass spectrum of **$tapH_2$** (top) and calculated mass (bottom).



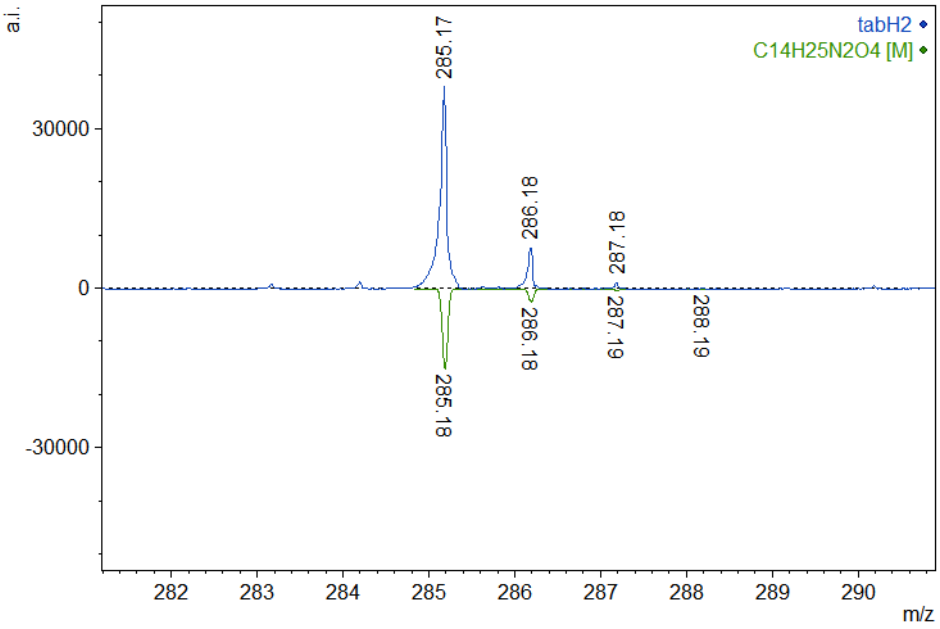
^{1}H and ^{13}C NMR spectra of **$tapH_2$** in $CDCl_3$.



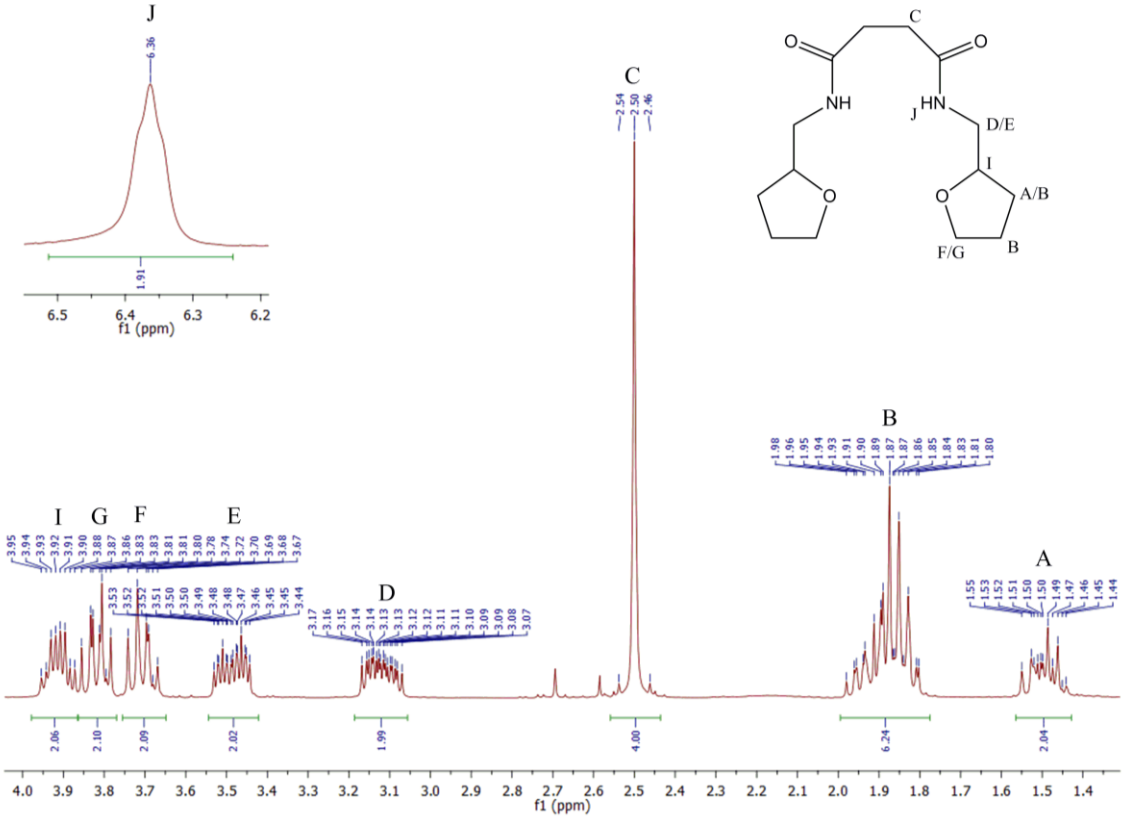

167.51
77.58
77.47
77.16 Chloroform-d
76.74
68.19
43.39
43.01
28.77
25.87
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

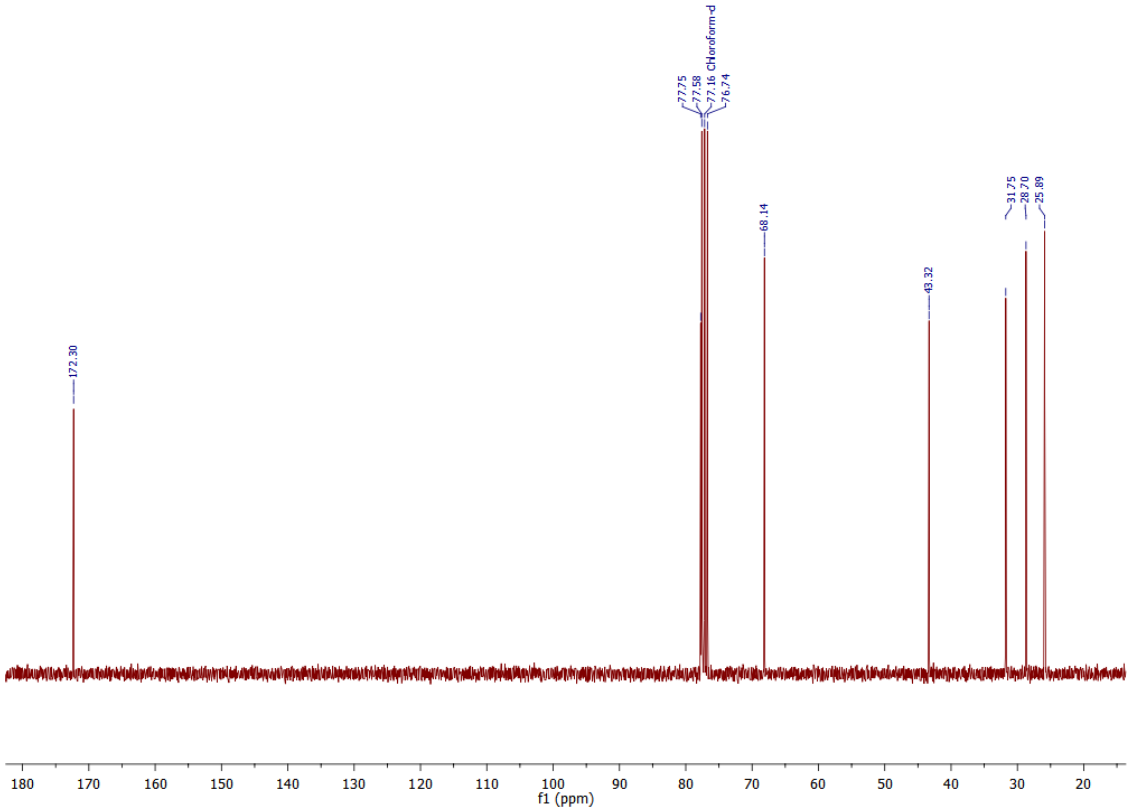
APPENDIX 9: $tabH_2$

MALDI-TOF mass spectrum of **$tabH_2$** (top) and calculated mass (bottom).



^{1}H and ^{13}C NMR spectra of **$tapH_2$** in $CDCl_3$.




77.75
77.58
77.16 CHloroform-d
76.74
172.30
68.14
43.32
31.75
28.70
25.89
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)